DEPARTMENT OF LABOR UNITED STATES OF AMERICA

Organic Vapor Sampling Group 3 (OVSG-3)
Diisocyanate Analytes Collected on Coated Glass Fiber Filters

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Method number: 5002

Version number: 1.0

Validated analytes:

Analyte	CAS No.
Hexamethylene diisocyanate	822-06-0
1,6-Hexamethylene diisocyanate homopolymer	28182-81-2
Isophorone diisocyanate	4098-71-9
Methylene bis(4-cyclohexylisocyanate)	5124-30-1
Methylene bisphenyl isocyanate (MDI)	101-68-8
Polymeric(methylene bisphenyl isocyanate)	9016-87-9
Toluene-2,4-diisocyanate (TDI)	584-84-9
Toluene-2,6-diisocyanate	91-08-7

Procedure: Collect samples by drawing workplace air containing specified diisocyanate vapors (and in some cases aerosols) through a glass fiber filter coated with 1 mg of 1-(2-pyridyl)piperazine (1-2PP) contained in an open-face cassette. Specified analytes, which are not present as gas phase components may also be trapped on the filter. Extract samples with 90/10 (v/v) acetonitrile/dimethyl sulfoxide (ACN/DMSO) and analyze by liquid chromatography (LC), specifically ultra-high performance liquid chromatography (UHPLC), using a fluorescence (FLR) detector. The analytes listed above are compatible with the coated filter, extraction solvent, and analysis conditions of Method 5002, and may be sampled separately or together.

Recommended sampling time and sampling rate: 15 min at 1.0 L/min (15 L)

Special requirements: Store the coated glass fiber filters separated from support pads and cassettes at reduced temperature (2.0 °C – 8.0 °C) until sampling. Assemble samplers immediately before sampling.

Validation status: Data found in the respective method appendices have been subjected to the established validation procedures of the OSHA Method Development Team. The method is considered to be fully validated for all analytes so designated.

February 2021

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1 Introduction

For assistance with accessibility problems in using figures and illustrations presented in this method, please contact the Salt Lake Technical Center (SLTC) at (801) 233-4900. This procedure was designed and tested for internal use by OSHA personnel. Mention of any company name or commercial product does not constitute endorsement by OSHA.

This method harmonizes the sampling, sample preparation, and analysis of diisocyanate analytes collected on coated glass fiber filters in open-face cassettes that are extracted with 90/10 (v/v) ACN/DMSO. Validation data for each analyte are described in the relevant appendices.

2 Sampling Procedure

Follow all safety practices that apply to the work area where sampling occurs.

2.1 Apparatus

A three-piece 37-mm polystyrene cassette containing a glass fiber filter coated with 1 mg of 1-2PP[1] (coated GFF in Figure 1) and a support pad are required for sampling. Commercially available cassettes, filters, and support pads were purchased from SKC Inc. (catalog nos. 225-3250, 225-7, and 225-27 respectively) for method development. The 1-2PP coated filters with support pad and cassettes are provided to OSHA field activities through official sampling media procurement channels, and documentation accompanying the filters provides an expiration date. Store unused filters at reduced temperature (2.0 ˚C – 8.0 ˚C) prior to use, and discard filters when expiration date is exceeded. All filters held within cassettes submitted for analysis (including field blanks) should be from the same lot.

A personal sampling pump calibrated to within ±5.0% of the recommended flow rate with a representative sampling device in-line is used to draw air through an open face cassette. When possible, sample over the duration specified.

2.2 Reagents

None Required.

2.3 Technique

Immediately before sampling, assemble the sampler as shown in Figure 1. The polystyrene top is used to fully seat the polystyrene spacer ring against the coated GFF. Then remove both end plugs and the polystyrene top from the three-piece cassette to sample in the open-face mode. Save the end plugs and polystyrene top for replacement after open-face sampling.

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[1] A coated filter was created by applying 0.500 mL of a solution of 2.0 mg/mL 1-2PP in methylene chloride to a glass fiber filter. Wet filters were allowed to air dry for 30 min before placing them in a jar, where residual methylene chloride was removed by applying vacuum to the jar. The 1-2PP solution should be prepared and used within 4 hours. The coated filters expire after 6 months from preparation date.

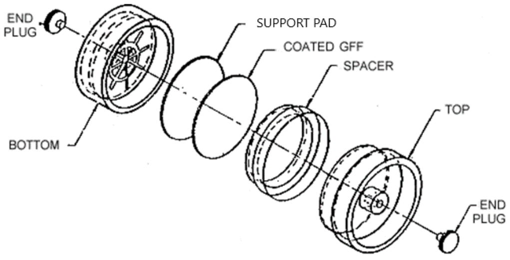

Figure 1. Diisocyanate sampler assembly.

Attach the cassette to the sampling pump so that the cassette is in an approximately vertical position with the inlet facing down in the worker's breathing zone during sampling. Position the sampling pump, cassette, and tubing so they do not impede worker performance or safety of an employee being sampled. The air being sampled should not pass through any hose or tubing before entering the open face of the sampling cassette.

Sample at 1.0 L/min for 15 min (15 L) for all analytes.

After sampling for the appropriate time, close each cassette with plugs and polystyrene top. Seal each sample end-to-end with a Form OSHA-21 as soon as possible.

Submit at least one field blank sample with each set of samples. Handle the field blank sample in the same manner as the other samples except draw no air through it.

Record sample air volume (liters), sampling time (min), and sampling rate (L/min) for each sample, along with any potential interference on the Form OSHA-91A.

Submit samples to the laboratory for analysis as soon as possible after sampling. If a delay is unavoidable, store the samples in a refrigerator as a precaution.

3 Analytical Procedure

3.1 Apparatus

- Mechanical vial rotator
- One liter amber glass solvent dispenser capable of dispensing 3.00 mL
- Syringes (10 and 50-µL)
- Class A volumetric flasks (10, 25, 1000 and 2000-mL)
- Class A graduated cylinder to deliver (100-mL)
- Class A volumetric pipette (1, 5, and 10-mL)
- Clear glass vials with polytetrafluoroethylene (PTFE)-lined screw caps (30-mL)
- Amber glass vials with PTFE-lined screw caps (2 and 4-mL)
- 0.2-µm PTFE syringe filters
- 47-mm, 0.45-µm PTFE filters
- UHPLC instrument with fluorescence detector

3.2 Reagents

- Toluene-2,4-diisocyanate (TDI, 95%, reagent grade or better)
- Toluene-2,6-diisocyanate (97%, reagent grade or better)
- Hexamethylene diisocyanate (98%, reagent grade or better)
- Methylene bisphenyl isocyanate (MDI, 98%, reagent grade or better)
- Isophorone diisocyanate (97.5%, reagent grade or better)
- Methylene bis(4-cyclohexylisocyanate) (90%, reagent grade or better)
- Polymeric 4,4'-methylenediphenyl diisocyanate (reagent grade or better)
- 1,6-Hexamethylene diisocyanate homopolymer (reagent grade or better)
- Methylene chloride ($MeCl_2$, reagent grade or better)
- Dimethyl sulfoxide (DMSO, reagent grade or better)
- Acetonitrile (ACN, reagent grade or better)
- 1-(2-Pyridyl)piperazine (1-2PP, 99%, reagent grade or better)
- Ammonium acetate (NH_4OAc, reagent grade or better)
- Phosphoric acid, (H_3PO_4, 85%, reagent grade or better)
- Deionized (DI) water, 18 MΩ-cm

3.3 Reagent Preparation

Extraction solvent (90/10 (v/v) ACN/DMSO): To a 1000-mL volumetric flask add approximately 800 mL of ACN, and exactly 100 mL of DMSO, then add ACN to the mark. Immediately mix the solution and transfer to an amber glass solvent dispenser.

Eluent A: Prepare 2 L of buffer by weighing out 7.71 g of NH_4OAc (correct for purity) into a 2-L volumetric flask containing 1400 mL of DI water 18 MΩ-cm. Add 500 µL of H_3PO_4 and 600 mL of ACN. Bring to the mark with DI water 18 MΩ-cm. Filter through a 47-mm 0.45-µm polytetrafluoroethylene (PTFE) filter. Mix thoroughly and wait for the solution to equilibrate (~15 min). Verify the pH (6.4 ± 0.2) of the solution with a calibrated pH meter. If the pH of the solution is outside the specified range, do not try to adjust, discard the eluent and prepare again.

Eluent B: ACN.

3.4 Standard Preparation

Use commercially available diisocyanate 1-2PP derivatives, with known purity, when possible and prepare standards as described in procedure A. If a diisocyanate derivative solution is not commercially available, synthesize diisocyanate 1-2PP derivatives using a modification[2] of the procedure described by Goldberg et al.,[3] or make standards using procedure B.

Preparation of calibration standards (procedure A: derivatized):

Prepare calibration standards by pipetting diisocyanate 1-2PP derivative solution into a 25-mL volumetric flask containing approximately 10 mL of extraction solvent. Fill to the mark with extraction solvent, mix, and transfer to a 30-mL vial. Matrix match the calibration standards by adding one coated filter per 3.00 mL of standard solution, mix and equilibrate for at least 1 hour. Then filter solution using a 0.2-µm PTFE filter. For analysis, transfer aliquots of the calibration standard to 2-mL glass autosampler vials. Prepare separate calibration standards for the polymers due to the presence of monomers in the polymer standards. Store all standards at reduced temperature (-20 °C). If sample concentrations are greater than the range of prepared standards, dilute high samples with extraction solvent and reanalyze the diluted samples.

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[2] Burright, D. Toluene-2,4-diisocyanate (OSHA Method 42), 1989. United States Department of Labor, Occupational Safety & Health Administration Web site. https://www.osha.gov/dts/sltc/methods/organic/org042/org042.html (accessed July 2020).

[3] Goldberg, P.A.; Walker, R.F.; Ellwood, P.A.; Hardy, H.L. Determination of trace atmospheric isocyanate concentrations by reversed-phase high-performance liquid chromatography using 1-(2-pyridyl)piperazine reagent. J. Chromatography A**. 1981**, 212, 93.

Preparation of calibration standards (procedure B: neat):
Prepare intermediate diisocyanate solutions by spiking microliter amounts or weighing neat diisocyanates into volumetric flasks containing methylene chloride solvent. Fill to the mark with methylene chloride solvent and mix. Prepare calibration standards by injecting microliter amounts of the intermediate diisocyanate solutions onto 1-2PP coated filters in 4-mL vials. After 4 hours, add 3.00 mL of extraction solvent to each vial and rotate for 1 hour. Filter the extracted solution using a 0.2-µm PTFE syringe filter into a 2-mL auto sampler vial. Seal the vial with a PTFE-lined cap. If sample concentrations are greater than the range of prepared standards, dilute high samples with extraction solvent and reanalyze the diluted samples.

3.5 Sample Preparation

Open a cassette and transfer the glass fiber filter into a 4-mL vial so that the filter is flat against the inside surface of the vial, not folded or crumpled. Place the side of the filter that faced the sampled atmosphere so that it faces the extraction solvent. Discard support pad and cassette.

Add 3.00-mL of extraction solvent to each vial and immediately seal with PTFE-lined caps.

Extract samples by rotating for 1 hour.

Filter the extracted solution using a 0.2-µm PTFE syringe filter into a 2-mL auto sampler vial and immediately seal the vial with a PTFE-lined cap.

3.6 Analysis

Analyze samples using a UHPLC instrument and the analytical parameters described below. For each analyte, construct a weighted least-squares linear regression curve by plotting response of standard injections versus micrograms of the stoichiometrically equivalent underivatized analyte per sample. A weighted linear least-squares curve using x^{-2} weight can be used to minimize the influence of heteroscedasticity and improve the accuracy at the lower end of the regression curve. Confirm the presence of analytes when an OSHA Permissible Exposure Limit (PEL) value or other target concentration has been exceeded, as described in Section 3.8. See Figures 2 and 3 below for an example of chromatograms obtained from standards containing analyte mass concentrations equivalent to sampling the underivatized analyte for the recommended time with each analyte at its respective OSHA PEL or other suitable target concentration.

<u>LC parameters</u>

gradient:

time (min)	flow rate (mL/min)	eluent A (%)	eluent B (%)	curve
initial	0.7	100	0	initial
0.50	0.7	100	0	6
2.50	0.7	87	13	6
5.50	0.7	75	25	6
6.00	0.7	52	48	6
7.50	0.7	40	60	10
8.00	0.7	40	60	1
8.20	0.7	100	0	6
9.00	0.7	100	0	6

column: Acquity UPLC HSS T3 100 Å, 1.8-µm, 2.1 mm x 50 mm

column flow: 0.7 mL/min

column temperature: 40 ˚C

run time: 9 min

injection: 3.0 µL

retention times:
1.80 min - toluene-2,6-diisocyanate 1-2PP derivative
2.01 min - hexamethylene diisocyanate 1-2PP derivative
2.29 min - toluene-2,4-diisocyanate (TDI) 1-2PP derivative
3.41 min - isophorone diisocyanate 1-2PP derivative (peak 1)
4.02 min - 1,6-Hexamethylene diisocyanate homopolymer 1-2PP derivative (peak 1)
4.26 min - isophorone diisocyanate 1-2PP derivative (peak 2)
4.31 min - methylene bisphenyl isocyanate (MDI) 1-2PP derivative
4.96 min - methylene bis(4-cyclohexylisocyanate) 1-2PP derivative
5.23 min - 1,6-Hexamethylene diisocyanate homopolymer 1-2PP derivative (peak 2)
5.91 min - 1,6-Hexamethylene diisocyanate homopolymer 1-2PP derivative (peak 3)
6.08 min - polymeric 4,4'-methylenediphenyl diisocyanate 1-2PP derivative (peak 1)
6.41 min - polymeric 4,4'-methylenediphenyl diisocyanate 1-2PP derivative (peak 2)
6.52 min - polymeric 4,4'-methylenediphenyl diisocyanate 1-2PP derivative (peak 3)
6.66 min - polymeric 4,4'-methylenediphenyl diisocyanate 1-2PP derivative (peak 4)

<u>FLR detector</u>

wavelength: 240 nm excitation, 370 nm emission

sensitivity: 10000 (EUFS)

sampling rate: 10 points/sec

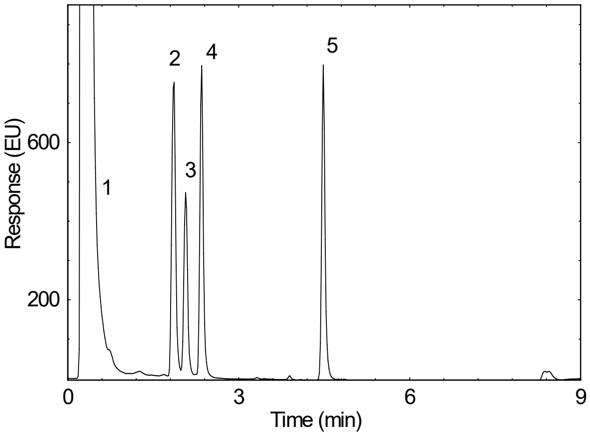

Figure 2. Example chromatogram. Peak labels: (1) 1-2PP/DMSO, (2) toluene-2,6-diisocyanate 1-2PP derivative, (3) hexamethylene diisocyanate 1-2PP derivative, (4) toluene-2,4-diisocyanate (TDI) 1-2PP derivative (5) methylene bisphenyl isocyanate (MDI) 1-2PP derivative.

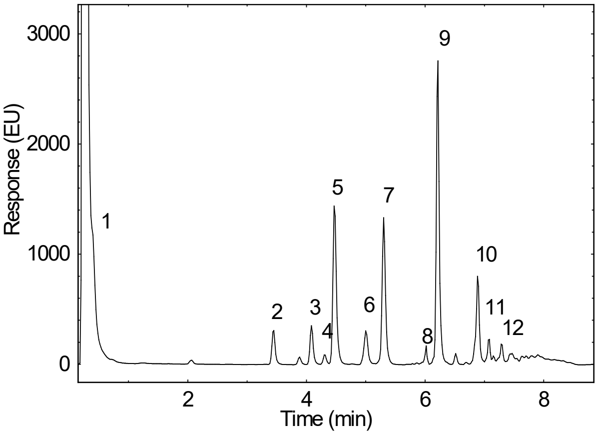

Figure 3. Example chromatogram. Peak labels: (1) 1-2PP/DMSO, (2) isophorone diisocyanate 1-2PP derivative (peak 1), (3) 1,6-Hexamethylene diisocyanate homopolymer 1-2PP derivative (peak 1), (4) isophorone diisocyanate 1-2PP derivative (peak 2), (5) methylene bisphenyl isocyanate (MDI) 1-2PP derivative, (6) methylene bis(4-cyclohexylisocyanate) 1-2PP derivative, (7) 1,6-Hexamethylene diisocyanate homopolymer 1-2PP derivative (peak 2), (8) 1,6-Hexamethylene diisocyanate homopolymer 1-2PP derivative (peak 3), (9) polymeric 4,4'-methylenediphenyl diisocyanate 1-2PP derivative (peak 1), (10) polymeric 4,4'-methylenediphenyl diisocyanate 1-2PP derivative (peak 2), (11) polymeric 4,4'-methylenediphenyl diisocyanate 1-2PP derivative (peak 3), (12) polymeric 4,4'-methylenediphenyl diisocyanate 1-2PP derivative (peak 4).

3.7 Calculations

Calculate the micrograms recovered per sample (m) for each analyte. If diisocyanate 1-2PP derivative was used to prepare calibration standards, convert the mass to the non-derivatized diisocyanates. For any analyte with multiple peaks, create a single curve by summing all the relevant peaks to determine m. Correct m for each sample by subtracting the mass of analyte (if any) found on the sample blank. The analyte air concentration (C) is calculated in mass per volume units (mg/m^3) using Equation 1, where V is the volume of air sampled (L), and E_E is the extraction efficiency expressed in decimal format.

$$C=\frac{m}{VE_E} \qquad \text{Equation 1}$$

The air concentration (C_{ppm}) in terms of parts of analyte vapor per million parts of air (ppm) is obtained using Equation 2, where C is the air concentration with mass per volume units (mg/m^3) calculated using Equation 1, V_M is the molar volume of an ideal gas or vapor at 25 °C and 760 Torr (24.46 L/mol), and M is the analyte molar mass (g/mol).

$$C_{ppm}=\frac{CV_M}{M} \qquad \text{Equation 2}$$

Values for E_E, obtained during validation studies, and M are listed in Table 1 along with the OSHA Integrated Management Information System (IMIS) numbers for each analyte.

Table 1. Molar mass, extraction efficiencies, and OSHA Integrated Management Information System (IMIS) numbers of Method 5002 analytes.

analytes	*M* (g/mol)	E_E	IMIS
Toluene-2,4-diisocyanate (TDI)	174.16	0.983	2470
Toluene-2,6-diisocyanates	174.16	0.975	T177
Hexamethylene diisocyanate	168.20	0.969	1377
Methylene bisphenyl diisocyanate (MDI)	250.25	0.991	1073
Isophorone diisocyanate	222.28	1.016	1539
Methylene bis(4-cyclohexylisocyanate)	262.35	0.998	2651
1,6-Hexamethylene diisocyanate homopolymer	478.0	1.005	H130
Polymeric-4,4'-methylenediphenyl diisocyanate	400.0[a]	1.014	P125

[a] Molar mass for polymeric 4,4'-methylenediphenyl diisocyanate is given as an example, always use the molar mass provided by the supplier.

3.8 Qualitative Analysis

When necessary, the identity of an analyte peak can be confirmed by LC-spectral library matching using photo diode array (PDA) absorption spectra or liquid chromatography-mass spectrometry (LC-MS) analysis. Confirm the presence of an analyte by matching the retention time and PDA spectral pattern or LC-MS spectra with those of a standard at a similar concentration.

3.8.1 PDA Spectral Library Matching

The analytical parameters described below can be used to produce PDA absorption spectra to verify the identity or purity of an analyte peak by spectral library matching. See Figures 4 through 13 below for example PDA chromatograms and absorption spectra for eight diisocyanate 1-2PP derivatives obtained from standards containing analyte derivative mass concentrations equivalent to sampling the underivatized analyte for the recommended time with each analyte at its respective OSHA PEL or other suitable target concentration.

LC parameters

gradient:

time (min)	flow rate (mL/min)	eluent A (%)	eluent B (%)	curve
initial	0.7	100	0	initial
0.50	0.7	100	0	6
2.50	0.7	87	13	6
5.50	0.7	75	25	6
6.00	0.7	52	48	6
7.50	0.7	40	60	10
8.00	0.7	40	60	1
8.20	0.7	100	0	6
9.00	0.7	100	0	6

column: Acquity UPLC HSS T3 100 Å, 1.8-µm, 2.1 mm x 50 mm

column flow: 0.7 mL/min

column temperature: 40 °C

run time: 9 min

injection: 3.0 µL

retention times:
1.80 min - toluene-2,6-diisocyanate 1-2PP derivative
2.01 min - hexamethylene diisocyanate 1-2PP derivative
2.29 min - toluene-2,4-diisocyanate (TDI) 1-2PP derivative
3.41 min - isophorone diisocyanate 1-2PP derivative (peak 1)
4.02 min - 1,6-Hexamethylene diisocyanate homopolymer 1-2PP derivative (peak 1)
4.26 min - isophorone diisocyanate 1-2PP derivative (peak 2)
4.31 min - methylene bisphenyl isocyanate (MDI) 1-2PP derivative
4.96 min - methylene bis(4-cyclohexylisocyanate) 1-2PP derivative
5.23 min - 1,6-Hexamethylene diisocyanate homopolymer 1-2PP derivative (peak 2)
5.91 min - 1,6-Hexamethylene diisocyanate homopolymer 1-2PP derivative (peak 3)
6.08 min - polymeric 4,4'-methylenediphenyl diisocyanate 1-2PP derivative (peak 1)
6.41 min - polymeric 4,4'-methylenediphenyl diisocyanate 1-2PP derivative (peak 2)
6.52 min - polymeric 4,4'-methylenediphenyl diisocyanate 1-2PP derivative (peak 3)
6.66 min - polymeric 4,4'-methylenediphenyl diisocyanate 1-2PP derivative (peak 4)

PDA detector

absorbance: scan 214 – 400 nm

absorbance: single wavelength 263 nm

sampling rate: 10 points/sec

resolution: 4.8 nm

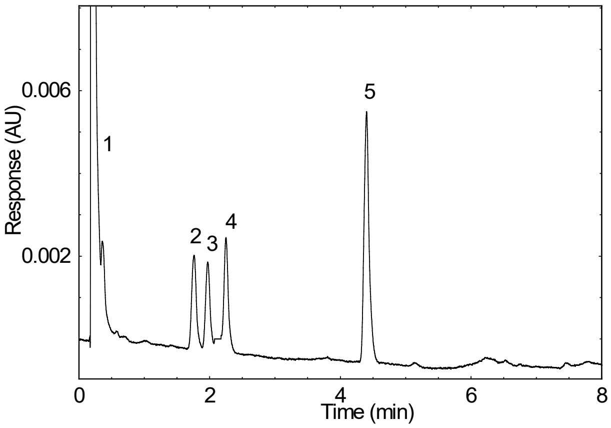

Figure 4. Example chromatogram. Peak labels: (1) 1-2PP/DMSO, (2) toluene-2,6-diisocyanate 1-2PP derivative, (3) hexamethylene diisocyanate 1-2PP derivative, (4) toluene-2,4-diisocyanate (TDI) 1-2PP derivative (5) methylene bisphenyl isocyanate (MDI) 1-2PP derivative.

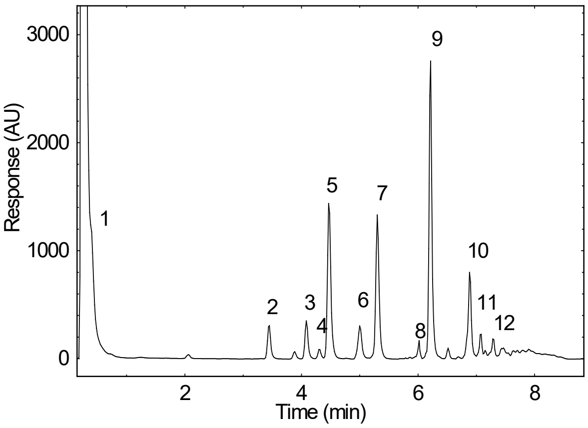

Figure 5. Example chromatogram. Peak labels: (1) 1-2PP/DMSO, (2) isophorone diisocyanate 1-2PP derivative (peak 1), (3) 1,6-Hexamethylene diisocyanate homopolymer 1-2PP derivative (peak 1), (4) isophorone diisocyanate 1-2PP derivative (peak 2), (5) methylene bisphenyl isocyanate (MDI) 1-2PP derivative, (6) methylene bis(4-cyclohexylisocyanate) 1-2PP derivative, (7) 1,6-Hexamethylene diisocyanate homopolymer 1-2PP derivative (peak 2), (8) 1,6-Hexamethylene diisocyanate homopolymer 1-2PP derivative (peak 3), (9) polymeric 4,4'-methylenediphenyl diisocyanate 1-2PP derivative (peak 1), (10) polymeric 4,4'-methylenediphenyl diisocyanate 1-2PP derivative (peak 2), (11) polymeric 4,4'-methylenediphenyl diisocyanate 1-2PP derivative (peak 3), (12) polymeric 4,4'-methylenediphenyl diisocyanate 1-2PP derivative (peak 4).

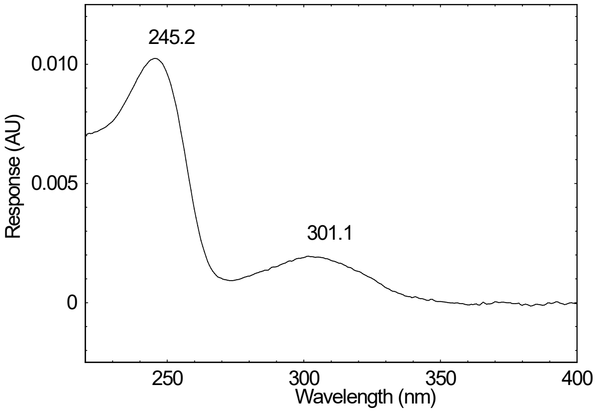

Figure 6. PDA-absorbance spectrum for the toluene-2,4-diisocyanate (TDI) 1-2PP derivative.

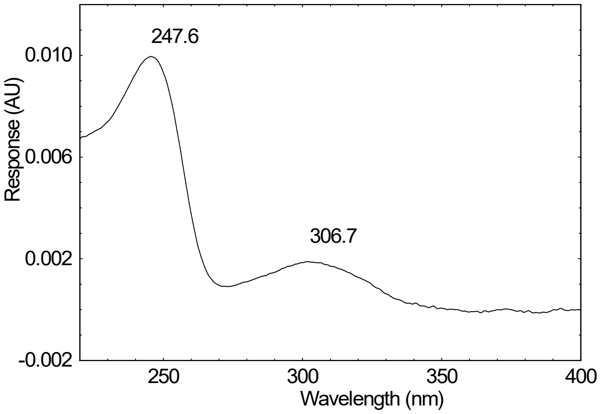

Figure 7. PDA absorbance spectrum for the hexamethylene diisocyanate 1-2PP derivative.

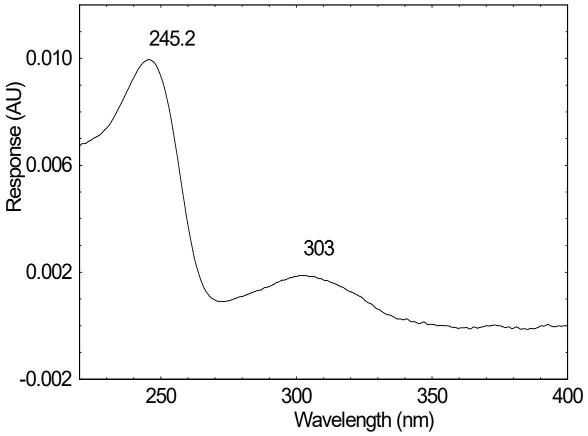

Figure 8. PDA absorbance spectrum for the toluene-2,6-diisocyanate 1-2PP derivative.

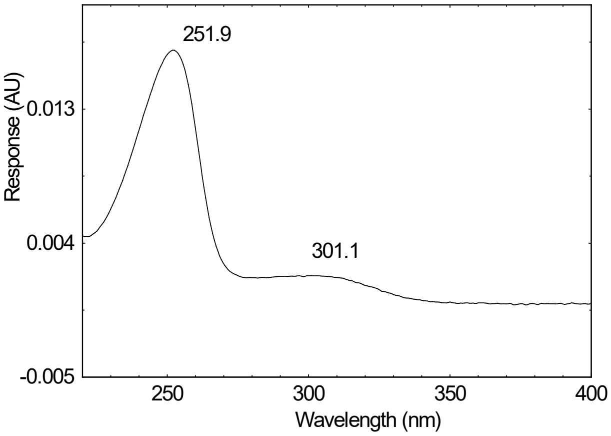

Figure 9. PDA absorbance spectrum for the methylene bisphenyl isocyanate (MDI) 1-2PP derivative.

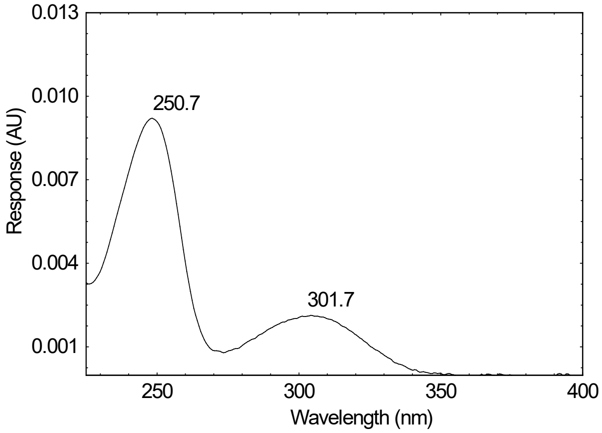

Figure 10. PDA absorbance spectrum for the 1,6-Hexamethylene diisocyanate homopolymer polymer 1-2PP derivative.

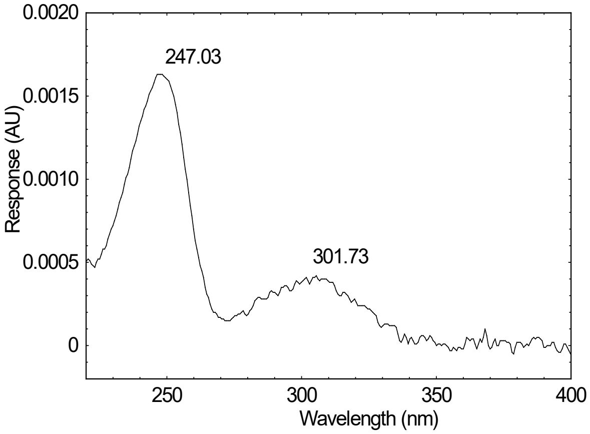

Figure 11. PDA absorbance spectrum for the isophorone diisocyanate 1-2PP derivative.

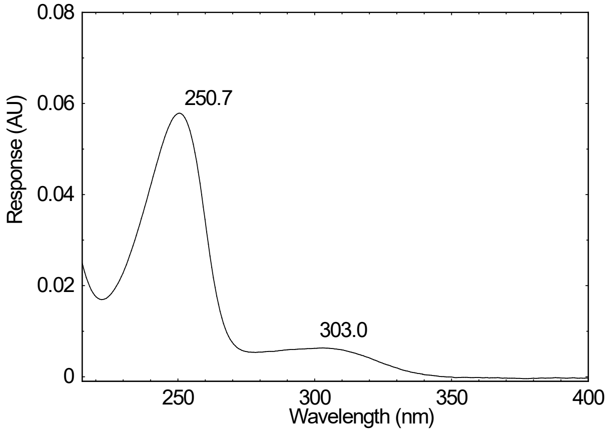

Figure 12. PDA absorbance spectrum for the methylene bis(4-cyclohexylisocyanate) 1-2PP derivative.

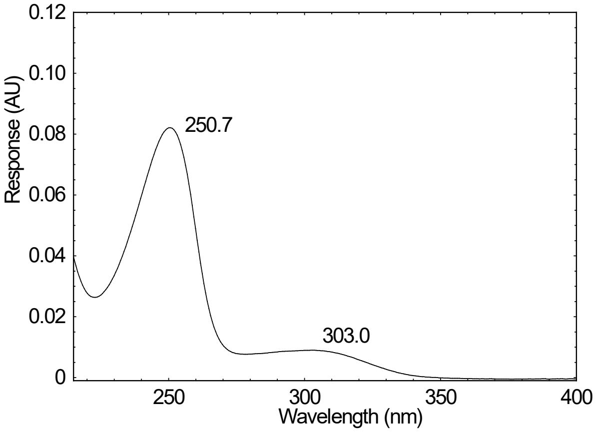

Figure 13. PDA absorbance spectrum for the polymeric 4,4'-methylenediphenyl diisocyanate 1-2PP derivative.

3.8.2 LC-MS Analysis

The LC parameters for LC-MS analysis are described below. See Figures 14 to 27 for Selective Ion Recording (SIR) chromatograms and mass spectra for seven diisocyanate 1-2PP derivative standards at concentrations equivalent to those that would be obtained by sampling for the recommended time, with each analyte at its respective OSHA PEL or other suitable target concentration. The molar mass values for the diisocyanate 1-2PP derivatives are calculated by adding the molar mass of a specific diisocyanate and that of any 1-2PP derivatizing agent added. For example, toluene-2,4-diisocyanate (TDI) (*M* = 174.16 g/mol) derivatized with two equivalents of 1-2PP (*M* = 163.22 g/mol), gives the molar mass of the toluene-2,4-diisocyanate (TDI) 1-2PP derivative as 500.6 g/mol. 1,6-Hexamethylene diisocyanate homopolymer and polymeric 4,4'-methylenediphenyl diisocyanate are derivatized with three equivalents of 1-2PP. All other diisocyanates are derivatized with two equivalents of 1-2PP. It is important to note that phosphoric acid should not be used in LC-MS. The phosphate and other acids with high boiling point can deposit in the source and plug the nebulizer thus requiring frequent cleaning and maintenance. Use acetic acid to prepare eluent buffer for LC-MS analysis.

Eluent A1: Prepare 2-L of buffer by weighing out 7.71g of NH_4OAc (correct for purity) into a 2-L volumetric flask containing 1400 mL of DI water 18 MΩ-cm. Add 500 µL of acetic acid and 600 mL of ACN. Bring to the mark with DI water 18 MΩ-cm. Filter through a 47-mm PTFE 0.45-µm filter. Mix thoroughly and wait for the solution to equilibrate (~15 min). Verify the pH (6.4 ± 0.2) of the solution with a calibrated pH meter. If the pH of the solution is outside the specified range, discard the eluent and prepare again.

Eluent B: Acetonitrile (ACN)

LC parameters

gradient:

time (min)	flow rate (mL/min)	eluent A1 (%)	eluent B (%)	curve
initial	0.6	100	0	initial
2.0	0.6	87	13	6
4.0	0.6	75	25	6
5.0	0.6	52	48	6
7.0	0.6	52	48	6
8.0	0.6	100	0	1

column:	Acquity UPLC BEH C18 130 Å, 1.8-µm, 2.1 mm x 50 mm
column flow:	0.6 mL/min
column temperature:	22.0 °C
injection volume:	2.0 µL
run time:	8.0 min
retention times:	1.34 min - toluene-2,6-diisocyanate 1-2PP derivative 1.43 min - hexamethylene diisocyanate 1-2PP derivative 1.66 min – toluene-2,4-diisocyanate (TDI) 1-2PP derivative 3.38 min - methylene bisphenyl isocyanate (MDI) 1-2PP derivative 4.02 min - 1,6-Hexamethylene diisocyanate homopolymer 1-2PP derivative (peak 1) 4.41 min - isophorone diisocyanate 1-2PP derivative (peak 1) 4.71 min - isophorone diisocyanate 1-2PP derivative (peak 2) 5.13 min - 1,6-Hexamethylene diisocyanate homopolymer 1-2PP derivative (peak 2) 5.39 min - polymeric 4,4'-methylenediphenyl diisocyanate 1-2PP derivative (peak 1) 6.63 min - polymeric 4,4'-methylenediphenyl diisocyanate 1-2PP derivative (peak 2)

	6.78 min - polymeric 4,4’-methylenediphenyl diisocyanate 1-2PP derivative (peak 3)

<u>MS function</u>

mode:	ESI
acquisition mode:	Parent scan
start mass:	*M* – 5
end mass:	*M* + 5

<u>MS source</u>

cone voltage:	40 V
collision energy:	0.0 eV
source temperature:	120 ˚C
desolvation temperature:	350 ˚C
desolvation gas flow:	750 L/Hr

<u>MS analyzer</u>

LM 1 resolution:	11.4
HM 1 resolution:	15.0
ion energy:	0.2 V
entrance:	30 V
collision:	3 V
exit:	30V
LM 2 resolution:	13.4
HM 2 resolution:	15.0
multiplier voltage:	650 V

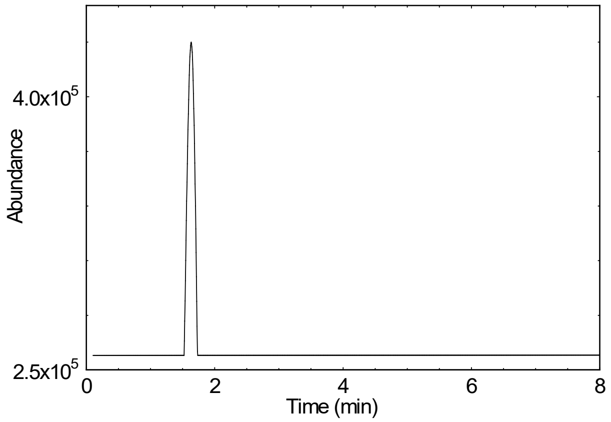

Figure 14. Selective Ion Recording (SIR) chromatogram for the toluene-2,4-diisocyanate (TDI) 1-2PP derivative.

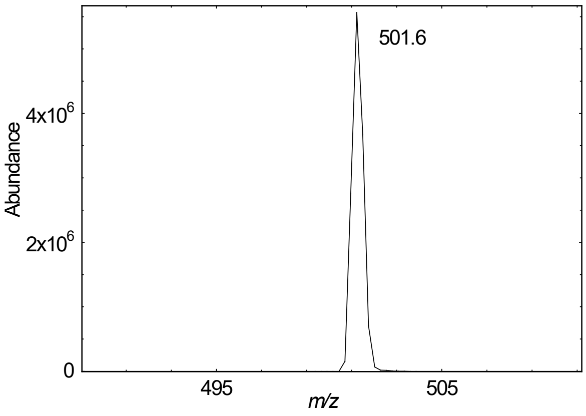

Figure 15. $[M + H]^+$ peak for the toluene-2,4-diisocyanate (TDI) 1-2PP derivative, calculated for $C_{27}H_{33}N_8O_2$ 501.6; found 501.6.

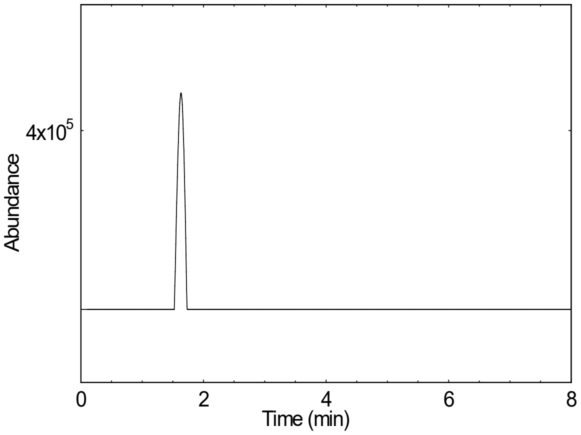

Figure 16. Selective Ion Recording (SIR) chromatogram for the hexamethylene diisocyanate 1-2PP derivative.

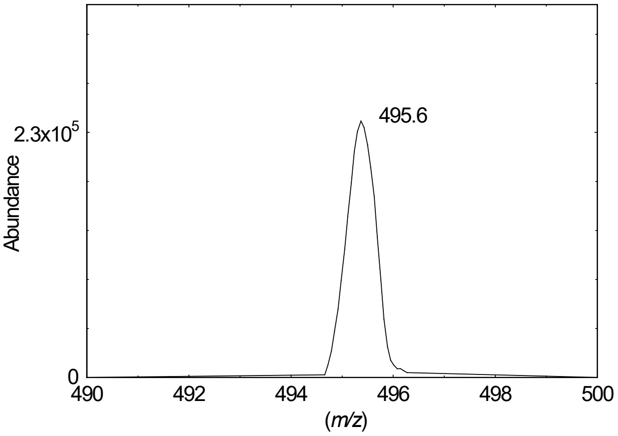

Figure 17. $[M + H]^+$ peak for the hexamethylene diisocyanate 1-2PP derivative, calculated for $C_{26}H_{39}N_8O_2$ 495.6; found 495.6.

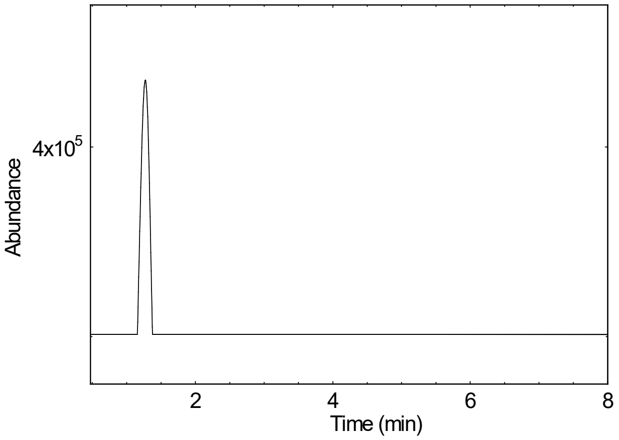

Figure 18. Selective Ion Recording (SIR) chromatogram for the toluene-2,6-diisocyanate 1-2PP derivative.

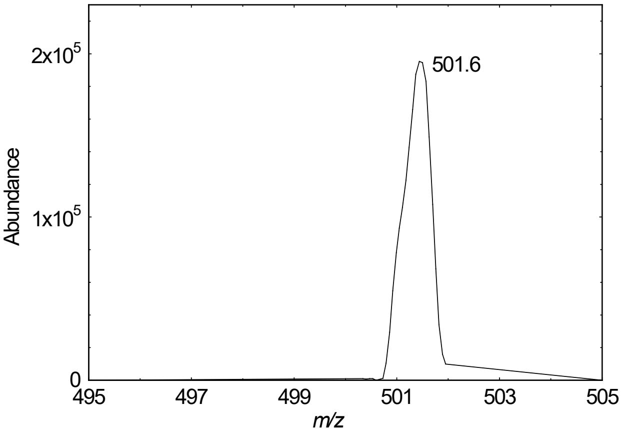

Figure 19. $[M + H]^+$ peak for the toluene-2,6-diisocyanate 1-2PP derivative, calculated for $C_{27}H_{33}N_8O_2$ 501.6; found 501.6.

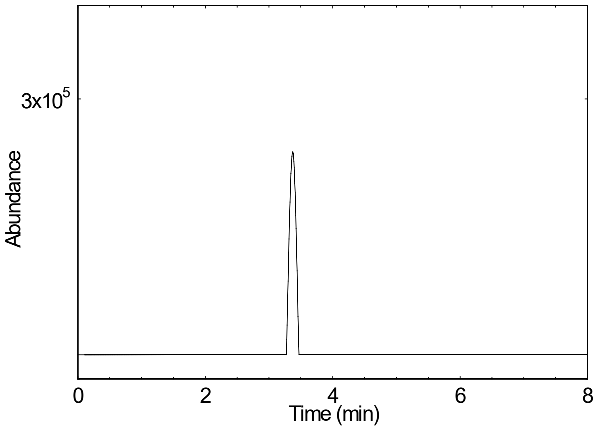

Figure 20. Selective Ion Recording (SIR) chromatogram for the methylene bisphenyl isocyanate (MDI) 1-2PP derivative.

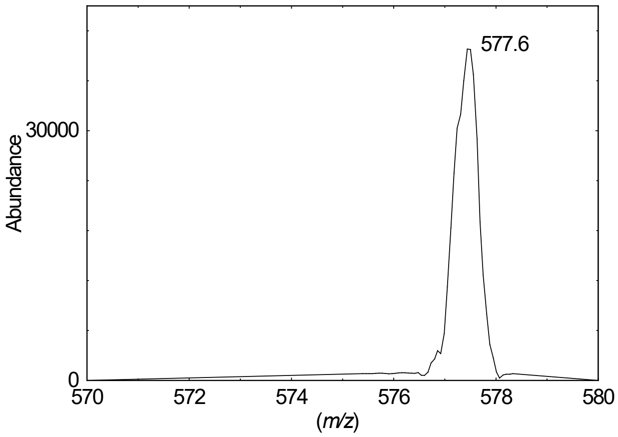

Figure 21. [M + H]$^+$ peak for the methylene bisphenyl isocyanate (MDI) 1-2PP derivative,
calculated for $C_{33}H_{37}N_8O_2$ 577.6; found 577.6.

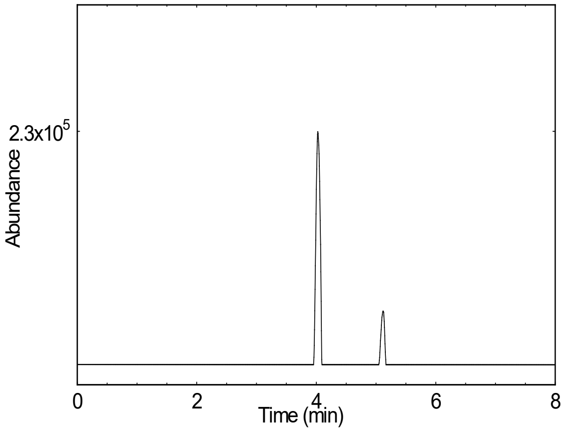

Figure 22. Selective Ion Recording (SIR) chromatogram for the 1,6-Hexamethylene diisocyanate homopolymer polymer 1-2PP derivatives.

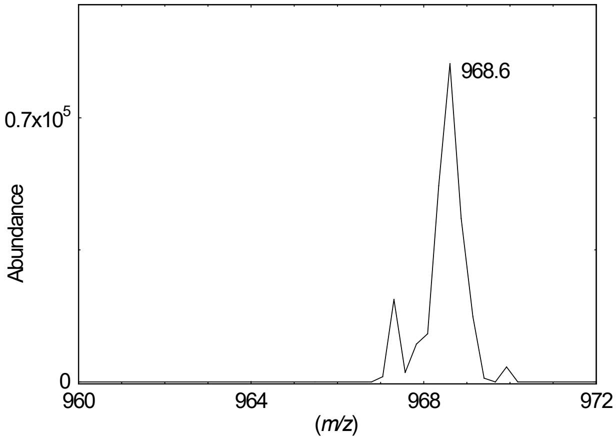

Figure 23. [M + H]$^+$ peak for the 1,6-Hexamethylene diisocyanate homopolymer 1-2PP derivative,
calculated 968.6[a]; found 968.6.
([a] calculated by adding molar mass of 1,6-Hexamethylene diisocyanate homopolymer (478.0 g/mol) to 3 × the molar mass of 1-2PP (163.22 g/mol). Additional oligomers may be present.)

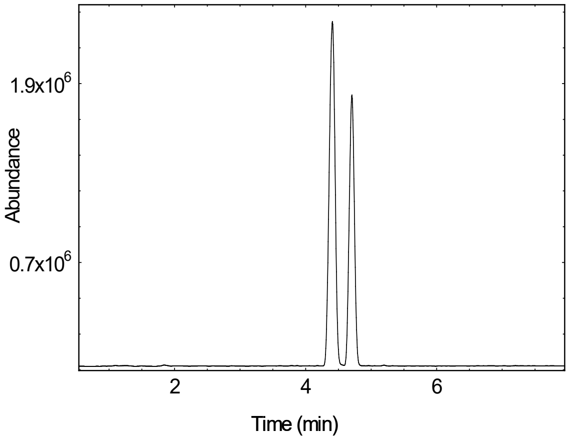

Figure 24. Selective Ion Recording (SIR) chromatogram of isophorone diisocyanate 1-2PP derivatives.

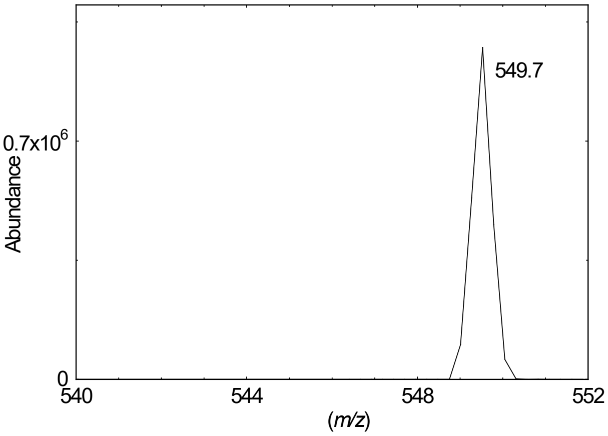

Figure 25. $[M + H]^+$ peak for the isophorone diisocyanate 1-2PP derivative, calculated for $C_{30}H_{45}N_8O_2$ 549.7; found 549.7.

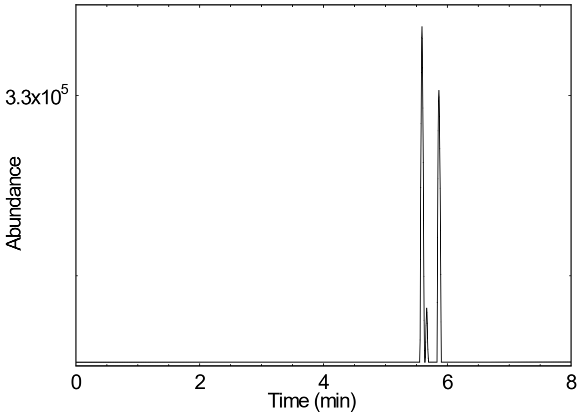

Figure 26. Selective Ion Recording (SIR) chromatogram of the polymeric 4,4'-methylenediphenyl diisocyanate 1-2PP derivatives.

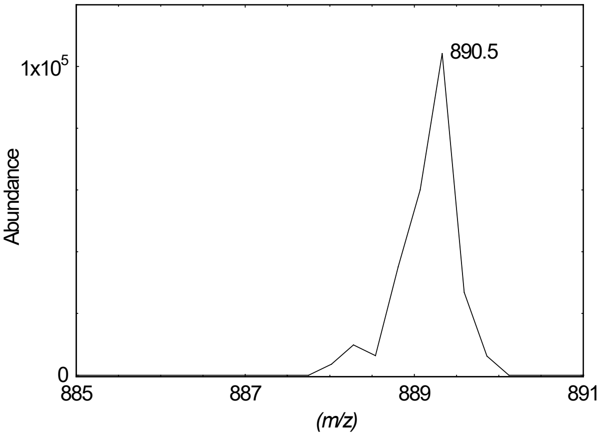

Figure 27. $[M + H]^+$ peak for the polymeric 4,4'-methylenediphenyl diisocyanate 1-2PP derivative, calculated for 890.6[a]; found 890.5.

([a] calculated by adding molar mass of polymeric 4,4'-methylenediphenyl diisocyanate (400 g/mol) to 3 × the molar mass of 1-2PP (163.22 g/mol). Additional oligomers may be present.)

OSHA 5002, Appendix A
Toluene-2,4-diisocyanate (TDI)

Version:	1.0
OSHA PEL:	0.02 ppm (0.14 mg/m^3) Ceiling, General Industry, Construction, Shipyard
ACGIH TLV:	0.001 ppm (0.007 mg/m^3) 8-Hour TWA, inhalable fraction and vapor 0.005 ppm (0.035 mg/m^3) 15-Minute STEL, inhalable fraction and vapor
Recommended sampling time and sampling rate:	15 min at 1.0 L/min (15 L)
Reliable quantitation limit:	0.18 ppb (1.3 μg/m^3)
Standard error of estimate:	5.8%
Status:	Fully validated. Method 5002 has been subjected to the established validation procedures of the Method Development Team for sampling and analysis of toluene-2,4-diisocyanate (TDI).

March 1989 (OSHA 42)
February 2021 (OSHA 5002)

Donald Burright
Radhakrishnan Ukkiramapandian

1 Introduction

1.1 Previous Methods used by OSHA for Sampling and Analysis of Toluene-2,4-Diisocyanate (TDI)

The specific analyte described in this appendix is toluene-2,4-diisocyanate (TDI) CAS No. 584-84-9. The methodologies described in this appendix for toluene-2,4-diisocyanate are based on OSHA Method 42.[1] That method requires the collection of samples using a 1-(2-pyridyl)piperazine (1-2PP)-coated glass fiber filter, extraction using 90/10 (v/v) acetonitrile/dimethyl sulfoxide (ACN/DMSO), and analysis by liquid chromatography using a fluorescence detector.

1.2 Changes to the Previously-Used Method

This appendix represents an update of OSHA Method 42[1], which was fully validated at the time it was published based on the validation guidelines in effect at that time. Compared to the previous method used, this method includes new analytical parameters and extraction solvent volume. Data presented from the previously used method are identified by the statement “Pre-existing data from OSHA Method 42[1] are presented in this section”. The changes were made to allow the standardized collection and analysis of toluene-2,4-diisocyanate (TDI) with other analytes found in Organic Vapor Sampling Group 3, described in OSHA Method 5002.

1.3 Validation Parameters

The procedures used to develop the method validation data are described in Validation Guidelines for Air Sampling Methods Utilizing Chromatographic Analysis.[2] Air concentrations listed in ppm are referenced to 25 °C and 760 Torr.

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[1] Burright, D. Toluene-2,4-diisocyanate (OSHA Method 42), 1989. United States Department of Labor, Occupational Safety & Health Administration Web site. https://www.osha.gov/dts/sltc/methods/organic/org042/org042.html (accessed July 2020).

[2] Eide, M.; Simmons, M.; Hendricks, W. Validation Guidelines for Air Sampling Methods Utilizing Chromatographic Analysis, 2010. United States Department of Labor, Occupational Safety & Health Administration Web site. http://www.osha.gov/dts/sltc/methods/chromguide/chromguide.pdf (accessed July 2020).

The target concentration for method evaluation was the OSHA ceiling permissible exposure limit for toluene-2,4-diisocyanate.

2 Detection and Quantification

2.1 Detection Limit of the Analytical Procedure (DLAP)

The DLAP is the analyte mass introduced onto the chromatographic column that produces a response greater than 3× the standard error of estimate (DLAP $S_{y/x}$) divided by the slope of the line produced from analyses of ten analytical standards prepared with equally spaced increments of analyte derivative mass. The standards were prepared in such a way that the highest 1-2PP derivative standard concentration would produce a peak approximately 10 times the response of a reagent blank at or near the chromatographic retention time of the analyte derivative. The standards and a reagent blank were analyzed with the recommended analytical parameters described in OSHA Method 5002. The resulting data provided the DLAP $S_{y/x}$ and slope values for DLAP determination. Results obtained for these analyses are listed in Table A-1 and plotted in Figure A-1.

Table A-1. DLAP data for the toluene-2,4-diisocyanate (TDI) 1-2PP derivative (concentration and mass on column as the underivatized analyte).

concentration (ng/mL)	mass on column (pg)	area counts (μV·s)
0.00	0.00	0.00
0.659	1.98	36,230
1.32	3.96	62,660
1.98	5.94	106,900
2.64	7.92	128,800
3.29	9.87	146,800
3.95	11.8	180,900
4.61	13.8	224,200
5.27	15.8	228,100
5.93	17.8	283,000
6.59	19.8	288,300

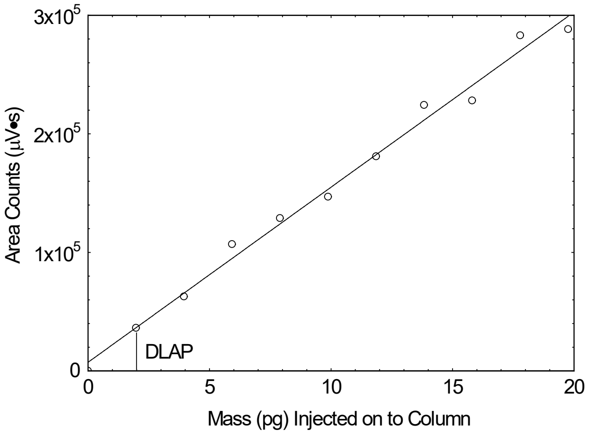

Figure A-1. Plot of data used to determine the DLAP for the toluene-2,4-diisocyanate (TDI) 1-2PP derivative (as the underivatized analyte, $y = 14{,}768x + 7399$, DLAP $S_{y/x}$ = 9965, DLAP = 2.02 pg).

2.2 Detection Limit of the Overall Procedure (DLOP) and Reliable Quantitation Limit (RQL)

The DLOP is the analyte mass introduced onto the chromatographic column that produces a response greater than 3× the standard error of estimate (DLOP $S_{y/x}$) divided by the slope of the line produced from analyses of ten samples prepared from coated filters spiked with equally spaced increments of analyte derivative mass. Coated filters were spiked in such a way that the highest 1-2PP derivative mass loading produced a peak approximately 10 times greater than that of a sample blank at or near the chromatographic retention time of the analyte derivative. The RQL is expressed as an air concentration that will provide sufficient analyte mass per sample to produce a response greater than 10× DLOP $S_{y/x}$ divided by the slope of the line described above. The spiked samplers and a sample blank were analyzed with the recommended analytical parameters described in OSHA Method 5002. The resulting data provided the DLOP $S_{y/x}$ and slope values for DLOP and RQL determinations. Results obtained from these analyses are listed in Table A-2, and plotted in Figure A-2.

Table A-2. DLOP and RQL data for the toluene-2,4-diisocyanate (TDI) 1-2PP derivative (mass per sample as the underivatized analyte).

mass per sample (ng/sample)	area counts (μV·s)
0.00	0.00
16.5	308,700
32.9	512,500
49.4	760,900
65.9	1,020,000
82.4	1,177,000
98.8	1,470,000
115	1,714,000
132	1,935,000
148	2,181,000
165	2,452,000

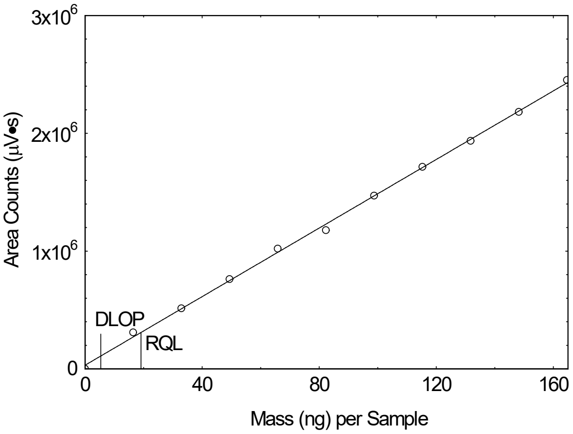

Figure A-2. Plot of data used to determine the DLOP and RQL for the toluene-2,4-diisocyanate (TDI) 1-2PP derivative (as the underivatized analyte, $y = 14{,}557x + 31{,}270$, DLOP $S_{y/x}$ = 28,034, DLOP = 5.78 ng/sample, RQL = 19.2 ng/sample or 0.180 ppb).

3 Analytical Precision Across the Calibration Range

Fifteen standards for the 1-2PP derivative were analyzed with the recommended analytical parameters described in OSHA Method 5002. These standards ranged from 0.1 to 2.0 times the analyte concentration in solvent that would be obtained from sampling the underivatized analyte for the recommended time at the target concentration. An ordinary least-squares linear regression curve was created by plotting the analyte mass per sample versus the corresponding area count of the analyte derivative peak. The resulting data provided the standard error of estimate (Calibration $S_{y/x}$) value across the calibration range, which provides an indication of the imprecision attributable to the instrumental analysis of the target analyte. Results from these analyses are listed in Table A-3, and plotted in Figure A-3.

Table A-3. Analytical precision data for the toluene-2,4-diisocyanate (TDI) 1-2PP derivative (concentration as the underivatized analyte).

× target	0.1×	0.5×	1×	1.5×	2.0×
concn (µg/sample)	0.234	1.17	2.33	3.41	4.63
area counts x 10^4 (µV·s)	334.0	1641	3281	4704	6462
	346.5	1643	3252	4709	6488
	337.4	1644	3246	4698	6469

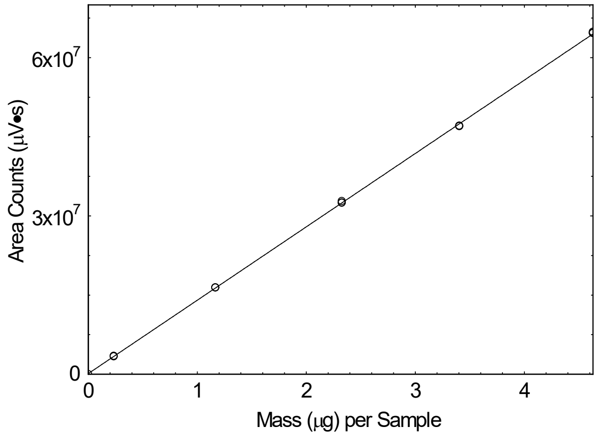

Figure A-3. Plot of data used to determine the precision of the analytical method for the toluene-2,4-diisocyanate (TDI) 1-2PP derivative (as the underivatized analyte, $y = 13{,}897{,}494x + 110{,}782$, Calibration $S_{y/x}$ = 282,645).

4 Sampler Storage Stability

Storage stability test samples were prepared by spiking the toluene-2,4-diisocyanate (TDI) 1-2PP derivative onto coated filters. The mass of the toluene-2,4-diisocyanate (TDI) 1-2PP derivative spiked was stoichiometrically equivalent to the mass of the underivatized analyte that would be sampled at the target concentration (calculated to be 0.0215 ppm) in air for 15 min at a flow rate of 1.0 L/min. Humid air (81.0% relative humidity at 22.0 °C) was then drawn through each filter following the recommended sampling parameters published in OSHA Method 5002. Eighteen such storage samples were prepared and three of these were analyzed on the same day that samples were created. The remaining fifteen samples were stored in a closed drawer at ambient temperature (about 22.0 °C). Three samples were selected and analyzed from those remaining at 3-4 day intervals. The results of these analyses (uncorrected for extraction efficiency) are provided in Table A-4 and in Figure A-4.

The recovery of the toluene-2,4-diisocyanate (TDI) 1-2PP derivative calculated from the regression line generated for the 18-day ambient storage test was 104.5%.

Table A-4. Sampler storage stability data for the toluene-2,4-diisocyanate (TDI) 1-2PP derivative

time (days)	ambient storage recovery (%)		
0	101.1	106.2	101.6
3	99.4	98.8	99.3
7	108.0	102.3	104.8
10	97.8	101.0	101.1
14	105.5	102.4	104.7
18	106.5	106.4	103.3

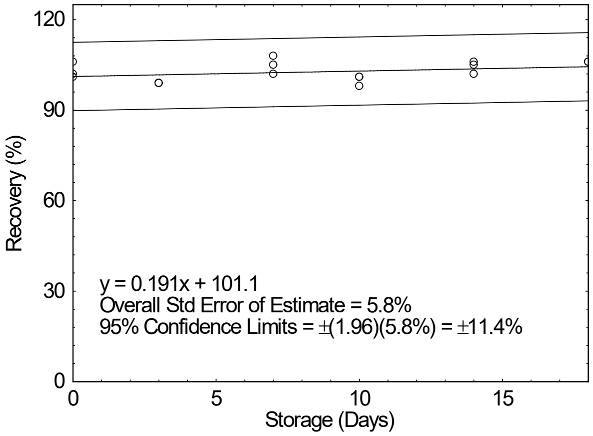

Figure A-4: Plot of ambient storage stability data for the toluene-2,4-diisocyanate (TDI) 1-2PP derivative.

5 Precision of the Overall Procedure

The overall standard error of estimate obtained from the ambient storage test analyses described in Section 4 and sampling pump variability were used to determine the precision of the overall procedure, where all aspects of sampling and analysis (sampling, filter handling and solvent extraction, and instrumental analysis) are considered. This value was obtained by taking the square root of the squared ambient storage stability standard error of estimate (Storage $S^2_{y/x}$) added to the squared sampling pump variability value (V^2_{SP}). The resulting precision of the overall procedure at the 95% confidence level for the ambient 18-day storage test (at the target concentration) for the toluene-2,4-diisocyanate (TDI) 1-2PP derivative was determined to be ±11.4% based on the observed ambient Storage $S_{y/x}$ value of 5.8% and V_{SP} value of 5.0%.

6 Recovery and Stability of Prepared Samples

Quantitative extraction is affected by the extraction solvent, the sampling medium, and the technique used to extract samples. The data presented demonstrate validity for the extraction solvent, sampling medium, and extraction technique described in OSHA Method 5002. If other combinations of these are to be used, testing must be completed to satisfy the requirements found in current OSHA sampling and analysis method validation guidelines. Acceptable testing results must be documented.

A value for extraction efficiency (E_E) was determined by spiking the toluene-2,4-diisocyanate (TDI) 1-2PP derivative onto four 1-2PP coated filters across a range of analyte derivative mass values that would be obtained from sampling the underivatized analyte at 0.1 to 2 times the target concentration value for 15 min. Four filters were also spiked in this fashion at the target concentration after drawing humid air (80.0% relative humidity at 21.0 °C) through these filters at 1.0 L/min for 15 min. All of the samples described above were analyzed the following day after being kept overnight at ambient temperature. The E_E value at the RQL was 119.8%, while that of the working range samples (excluding the samples through which humid air had been drawn) was 98.3%. The data are shown in Table A-5. Pre-loading filters with moisture ("wet" designation in the table) did not have an unacceptable effect on E_E.

Table A-5. Extraction efficiency data for the toluene-2,4-diisocyanate (TDI) 1-2PP derivative (µg per sample as the underivatized analyte).

level		sample number				
× target concn	µg per sample	1	2	3	4	mean
0.1	0.230	99.1	99.4	95.4	97.4	97.8
0.25	0.590	98.3	96.7	98.3	96.7	97.5
0.5	1.10	98.4	98.4	98.4	98.4	98.4
1.0	2.34	100.1	98.9	99.3	98.1	99.1
1.5	3.43	99.5	99.5	99.8	98.4	99.3
2.0	4.68	98.0	97.1	96.3	98.8	97.6
RQL	0.0200	121.0	121.0	121.0	116.1	119.8
1.0 (wet)	2.34	97.3	98.2	98.6	98.6	98.2
1.0 (dry)[a]	2.44	101.3	100.9	97.0	103.4	100.7
1.0 (wet)[a]	2.44	92.9	94.1	95.0	94.1	94.0

[a] Underivatized toluene-2,4-diisocyanate (TDI) spiked onto four replicate coated filters.

The stability of sample extracts prepared according to OSHA Method 5002 was examined by retaining the sample solvent extracts for the target concentration samples described immediately above. Two of the four vials were immediately recapped with new septa following the initial analyses, and again following each re-analysis event. The other two vials retained the original punctured septa throughout. All four vials were re-analyzed at 24, 48, and 72 hours after the initial analyses, with all vials remaining in an autosampler tray kept at 8.0 °C. Freshly prepared standards were used for each re-analysis event, and each septum (whether new or previously used) was punctured one time for each injection. The resulting data are shown in Table A-6.

Table A-6. Extracted sample stability data for the toluene-2,4-diisocyanate (TDI) 1-2PP derivative.

	punctured septa replaced recovery (%)		punctured septa retained recovery (%)	
time (days)	1	2	1	2
0	104.6	103.3	104.1	102.8
1	103.8	102.2	103.4	102.0
2	104.7	103.0	104.7	102.6
3	104.9	102.8	103.3	105.2

7 Sampler Capacity

Pre-existing data from OSHA Method 42[1] are presented in this section.

The sampling capacity of a coated filter was tested by performing a sample media analyte retention test. A filter to be spiked was mounted within a cassette in front of another coated filter, with a spacer separating the two filters. Six coated filters were liquid spiked with toluene-2,4-diisocyanate (TDI) 1-2PP derivative nominally four times the target concentration (calculated to be 0.0784 ppm). Air was drawn through these samplers with a flow rate of 1.0 L/min for 240 min. The relative humidity and temperature were 71% and 21.0 °C. Breakthrough was not observed after sampling for 240 min (corresponding to 240 liters). Data from six coated samplers, as shown in Table A-7, were used to determine the recommended sampling volume of 15 liters for toluene-2,4-diisocyanate (TDI) as described in OSHA Method 5002.

This volume corresponds to a 15 min sampling period, which is the maximum recommended sampling time regardless of breakthrough.

Table A-7. Retention data for the toluene-2,4-diisocyanate (TDI) 1-2PP derivative.

sample no.	air volume (L)	recovery front (%)	recovery back (%)
1	240	106.6	0.0
2	240	106.1	0.0
3	240	105.9	0.0
4	240	106.6	0.0
5	240	105.3	0.0
6	240	105.4	0.0

8 Low Humidity

Pre-existing data from OSHA Method 42[1] are presented in this section.

The effect of low humidity was tested by spiking underivatized toluene-2,4-diisocyanate (TDI) onto silanized glass wool placed in a glass tube or syringe directly upstream of a sampling cassette containing a 1-2PP coated filter. The mass of toluene-2,4-diisocyanate (TDI) spiked was nominally equivalent to the mass that would be sampled at fifteen times the target concentration (calculated to be 0.298 ppm) in air for 15 min at a flow rate of 1.0 L/min. Following spiking of the underivatized compound onto the glass wool, dry air (12.0% relative humidity at 21.0 °C) was drawn through each of two samplers thus prepared via the spiking system at a flow rate of 1.0 L/min for 200 min. After immediate analysis, results for the toluene-2,4-diisocyanate (TDI) 1-2PP derivative as a percentage of expected recovery were 94.4% and 92.9%.

9 Chemical Interference

The effect of potential chemical sampling interference was tested by spiking underivatized toluene-2,4-diisocyanate (TDI) onto silanized glass wool placed in a glass tube or syringe directly upstream of a sampling cassette containing a 1-2PP coated filter. The mass of toluene-2,4-diisocyanate (TDI) spiked was nominally equivalent to the mass that would be sampled at the target concentration (calculated to be 0.0229 ppm) in air for 15 min at a flow rate of 1.0 L/min. Underivatized hexamethylene diisocyanate and toluene-2,6-diisocyanate interferents were also spiked at masses corresponding to sampling these under the same conditions at concentrations of 0.0195 ppm and 0.0229 ppm respectively. Following spiking of the underivatized compounds onto the glass wool, humid air (81.0% relative humidity at 21.0 °C) was drawn through each of three cassette samplers thus prepared via the spiking system at a flow rate of 1.0 L/min for 15 min. After immediate analysis, results for the toluene-2,4-diisocyanate (TDI) 1-2PP derivative as a percentage of expected recovery were 95.8%, 94.5%, and 95.5%.

10 Analytical Method Reproducibility

Pre-existing data from OSHA Method 42[1] are presented in this section.

Samples were prepared by spiking five 1-2PP coated filters with the underivatized toluene-2,4-diisocyanate (TDI) in such a way that the mass of the analyte that would be sampled at the target concentration in air for 20 min at a sampling flow rate of 1.0 L/min (calculated to be 0.0223 ppm). Following this, 20 L of humidified air (80.0% relative humidity at 21.0 °C) was drawn through each filter in a cassette. The resulting samples were submitted to the OSHA Salt Lake Technical Center for analysis using the procedures described in OSHA Method 42 after refrigerated (-26.0 °C) storage for 6 days. The analytical results corrected for E_E are provided in Table A-8. No sample result for the toluene-2,4-diisocyanate (TDI) 1-2PP derivative fell outside the permissible bounds set by the precision of the overall procedure determined in Section 5 of this appendix.

Table A-8. Reproducibility data for the underivatized toluene-2,4-diisocyanate (TDI)

spiked (μg/sample)	recovered (μg/sample)	recovery (%)	deviation (%)
3.18	3.38	106.3	+6.3
3.18	3.29	103.5	+3.5
3.18	3.46	108.8	+8.8
3.18	3.38	106.3	+6.3
3.18	3.27	102.8	+2.8

11 Effect of Sampling a Low Concentration

A study has not been undertaken to verify the effect of sampling a low concentration of toluene-2,4-diisocyanate (TDI) vapor.

12 Estimation of Uncertainty

While systematic biases such as analyte storage loss are examined, and limits are placed on these, an estimation of uncertainty that encompasses both potential random and systematic error was not completed. Instead, the overall standard error of estimate was calculated from the random error inherent to the points about the regression line produced by the ambient storage test described in Section 5, as prescribed by the OSHA validation guidelines in use at the time OSHA Method 5002 was originally validated. See Section 5 of this appendix for details.

13 Controlled Test Atmosphere Procedure

A controlled test atmosphere containing toluene-2,4-diisocyanate (TDI) vapor was not generated.

OSHA 5002, Appendix B
Hexamethylene Diisocyanate

Version:	1.0
OSHA PEL:	None
ACGIH TLV:	0.005 ppm (0.035 mg/m^3) 8-Hour TWA
Recommended sampling time and sampling rate:	15 min at 1.0 L/min (15 L)
Reliable quantitation limit:	0.34 ppb (2.3 µg/m^3)
Standard error of estimate:	6.0%
Status:	Fully validated. Method 5002 has been subjected to the established validation procedures of the Method Development Team for sampling and analysis of hexamethylene diisocyanate.

March 1989 (OSHA 42)
February 2021 (OSHA 5002)

Donald Burright
Radhakrishnan Ukkiramapandian

1 Introduction

1.1 Previous Methods used by OSHA for Sampling and Analysis of Hexamethylene Diisocyanate

The specific analyte described in this appendix is hexamethylene diisocyanate CAS No. 822-06-0. The methodologies described in this appendix for hexamethylene diisocyanate are based on OSHA Method 42.[1] That method requires the collection of samples using a 1-(2-pyridyl)piperazine (1-2PP)-coated glass fiber filter, extraction using 90/10 (v/v) acetonitrile/dimethyl sulfoxide (ACN/DMSO), and analysis by liquid chromatography using a fluorescence detector.

1.2 Changes to the Previously-Used Method

This appendix represents an update of OSHA Method 42,[1] which was fully validated at the time it was published based on the validation guidelines in effect at that time. Compared to the previous method used, this method includes new analytical parameters and extraction solvent volume. Data presented from the previously used method are identified by the statement “Pre-existing data from OSHA Method 42[1] are presented in this section”. The changes were made to allow the standardized collection and analysis of hexamethylene diisocyanate with other analytes found in Organic Vapor Sampling Group 3, described in OSHA Method 5002.

1.3 Validation Parameters

The procedures used to develop the method validation data are described in Validation Guidelines for Air Sampling Methods Utilizing Chromatographic Analysis.[2] Air concentrations listed in ppm are referenced to 25 °C and 760 Torr. The target concentration for method evaluation was 0.02 ppm for hexamethylene diisocyanate.

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[1] Burright, D. hexamethylene diisocyanate (OSHA Method 42), 1989. United States Department of Labor, Occupational Safety & Health Administration Web site. https://www.osha.gov/dts/sltc/methods/organic/org042/org042.html (accessed July 2020).

[2] Eide, M.; Simmons, M.; Hendricks, W. Validation Guidelines for Air Sampling Methods Utilizing Chromatographic Analysis, 2010. United States Department of Labor, Occupational Safety & Health Administration Web site. http://www.osha.gov/dts/sltc/methods/chromguide/chromguide.pdf (accessed July 2020).

2 Detection and Quantification

2.1 Detection Limit of the Analytical Procedure (DLAP)

The DLAP is the analyte mass introduced onto the chromatographic column that produces a response greater than 3× the standard error of estimate (DLAP $S_{y/x}$) divided by the slope of the line produced from analyses of ten analytical standards prepared with equally spaced increments of analyte derivative mass. The standards were prepared in such a way that the highest 1-2PP derivative standard concentration would produce a peak approximately 10 times the response of a reagent blank at or near the chromatographic retention time of the analyte derivative. The standards and a reagent blank were analyzed with the recommended analytical parameters described in OSHA Method 5002. The resulting data provided the DLAP $S_{y/x}$ and slope values for DLAP determination. Results obtained for these analyses are listed in Table B-1 and plotted in Figure B-1.

Table B-1. DLAP data for the hexamethylene diisocyanate 1-2PP derivative (concentration and mass on column as the underivatized analyte).

concentration (ng/mL)	mass on column (pg)	area counts (μV·s)
0.00	0.00	0.00
0.826	2.48	26,100
1.65	4.95	43,430
2.48	7.43	58,330
3.30	9.91	80,970
4.13	12.4	95,130
4.95	14.9	128,400
5.78	17.3	133,200
6.60	19.8	145,600
7.43	22.3	171,000
8.26	24.8	181,600

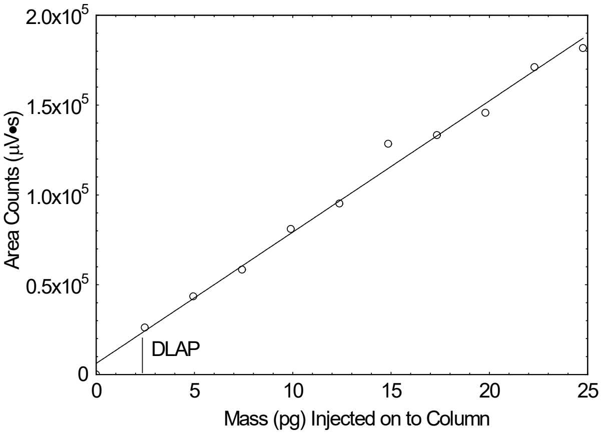

Figure B-1. Plot of data used to determine the DLAP for the hexamethylene diisocyanate 1-2PP derivative (as the underivatized analyte, $y = 7306x + 6192$, DLAP $S_{y/x} =$ 5762, DLAP = 2.37 pg).

2.2 Detection Limit of the Overall Procedure (DLOP) and Reliable Quantitation Limit (RQL)

The DLOP is the analyte mass introduced onto the chromatographic column that produces a response greater than 3× the standard error of estimate (DLOP $S_{y/x}$) divided by the slope of the line produced from analyses of ten samples prepared from coated filters spiked with equally spaced increments of analyte derivative mass. The samplers were spiked in such a way that the highest 1-2PP derivative mass loading produced a peak approximately 10 times greater than that of a sample blank at or near the chromatographic retention time of the analyte derivative. The RQL is expressed as an air concentration that will provide sufficient analyte mass per sample that produces a response greater than 10× DLOP $S_{y/x}$ divided by the slope of the line described above. The spiked samplers and a sample blank were analyzed with the recommended analytical parameters described in OSHA Method 5002. The resulting data provided the DLOP $S_{y/x}$ and slope values for DLOP and RQL determinations. Results obtained from these analyses are listed in Table B-2, and plotted in Figure B-2.

Table B-2. DLOP and RQL data for the hexamethylene diisocyanate 1-2PP derivative (mass per sample as the underivatized analyte).

mass per sample (ng/sample)	area counts (μV·s)
0.00	219,200
20.6	353,000
41.3	512,800
61.9	689,900
82.6	866,100
103	933,500
124	1,151,000
144	1,315,000
165	1,457,000
186	1,601,000
206	1,718,000

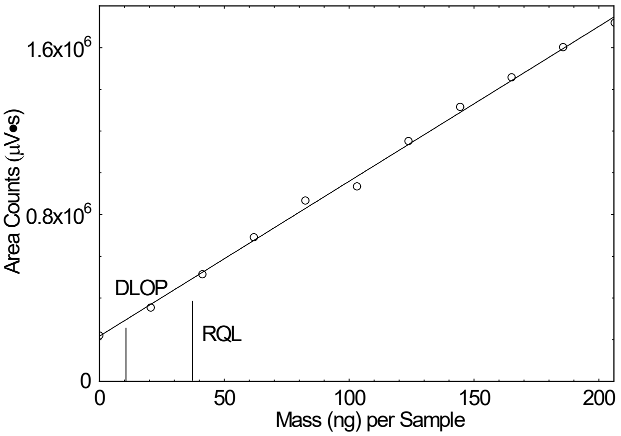

Figure B-2. Plot of data used to determine the DLOP and RQL for the hexamethylene diisocyanate 1-2PP derivative (as the underivatized analyte, $y = 7430x + 217{,}049$, DLOP $S_{y/x}$ = 26,341, DLOP = 10.6 ng/sample, RQL = 35.0 ng/sample or 0.339 ppb).

3 Analytical Precision Across the Calibration Range

Fifteen standards for the 1-2PP derivative were analyzed with the recommended analytical parameters described in OSHA Method 5002. These standards ranged from 0.1 to 2.0 times the analyte concentration in solvent that would be obtained from sampling the underivatized analyte for the recommended time at the target concentration. An ordinary least-squares linear regression curve was created by plotting the analyte mass per sample versus the corresponding area count of the analyte derivative peak. The resulting data provided the standard error of estimate (Calibration $S_{y/x}$) value across the calibration range, which provides an indication of the imprecision attributable to the instrumental analysis of the target analyte. Results from these analyses are listed in Table B-3, and plotted in Figure B-3.

Table B-3. Analytical precision data for the hexamethylene diisocyanate 1-2PP derivative (concentration as the underivatized analyte).

× target	0.1×	0.5×	1.0×	1.5×	2.0×
concn (μg/sample)	0.203	1.02	2.02	2.96	4.03
area counts x 10^4 (μV·s)	161.0	767.4	1530	2194	2993
	160.8	774.0	1529	2206	3046
	163.6	767.9	1508	2190	3035

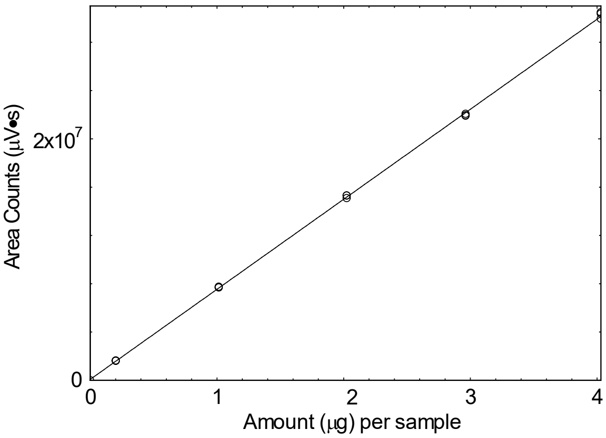

Figure B-3. Plot of data used to determine the precision of the analytical method for the hexamethylene diisocyanate 1-2PP derivative (as the underivatized analyte, $y = 7{,}456{,}938x + 89{,}097$, Calibration $S_{y/x}$ = 168,278).

4 Sampler Storage Stability

Storage stability test samples were prepared by spiking the hexamethylene diisocyanate 1-2PP derivative onto coated filters. The mass of the hexamethylene diisocyanate 1-2PP derivative spiked was stoichiometrically equivalent to the mass of the underivatized analyte that would be sampled at the target concentration (calculated to be 0.0217 ppm) in air for 15 min at a flow rate of 1.0 L/min. Humid air (81.0% relative humidity at 22.0 °C) was then drawn through each filter following the recommended sampling parameters published in OSHA Method 5002. Eighteen such storage samples were prepared and three of these were analyzed on the same day that samples were created. The remaining fifteen samples were kept in a closed drawer at ambient temperature (about 22.0 °C). Three samples were selected and analyzed from those remaining at 3-4 day intervals. The results of these analyses (uncorrected for extraction efficiency) are provided in Table B-4 and in Figure B-4.

The recovery of the hexamethylene diisocyanate 1-2PP derivative calculated from the regression line generated for the 18-day ambient storage test was 105.4%.

Table B-4. Sampler storage stability data for the hexamethylene diisocyanate 1-2PP derivative.

time (days)	ambient storage recovery (%)		
0	97.8	102.9	97.5
3	101.0	96.9	96.2
7	108.6	104.2	105.9
10	100.8	99.6	99.7
14	108.0	104.5	106.0
18	103.1	106.5	102.2

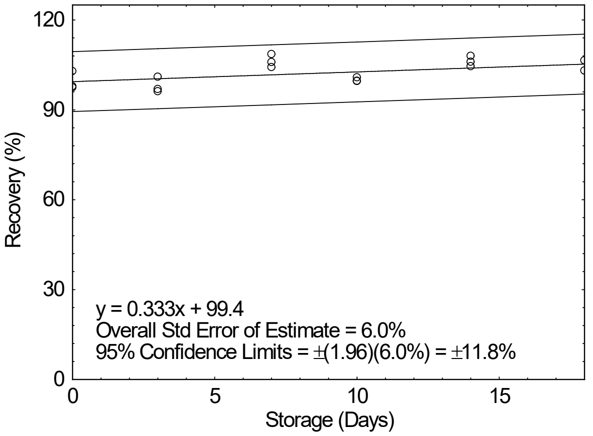

Figure B-4: Plot of ambient storage stability data for the hexamethylene diisocyanate 1-2PP derivative.

5 Precision of the Overall Procedure

The overall standard error of estimate obtained from the ambient storage test analyses described in Section 4 and sampling pump variability were used to determine the precision of the overall procedure, where all aspects of sampling and analysis (sampling, filter handling and solvent extraction, and instrumental analysis) are considered. This value was obtained by taking the square root of the squared ambient storage stability standard error of estimate (Storage $S^2_{y/x}$) added to the squared sampling pump variability value (V^2_{SP}). The resulting precision of the overall procedure at the 95% confidence level for the ambient 18-day storage test (at the target concentration) for the hexamethylene diisocyanate 1-2PP derivative was determined to be ±11.8% based on the observed ambient Storage $S_{y/x}$ value of 6.0% and V_{SP} value of 5.0%.

6 Recovery and Stability of Prepared Samples

Quantitative extraction is affected by the extraction solvent, the sampling medium, and the technique used to extract samples. The data presented demonstrate validity for the extraction solvent, sampling medium and extraction technique described in OSHA Method 5002. If other combinations of these are to be used, testing must be completed to satisfy the requirements found in current OSHA sampling and analysis method validation guidelines. Acceptable testing results must be documented.

A value for extraction efficiency (E_E) was determined by spiking the hexamethylene diisocyanate 1-2PP derivative onto four 1-2PP coated filters across a range of analyte derivative mass values that would be obtained from sampling the underivatized analyte at 0.1 to 2 times the target concentration value for 15 min. Four filters were also spiked in this fashion at the target concentration after drawing humid air (80.0% relative humidity at 21.0 °C) through these filters at 1.0 L/min for 15 min. All of the samples described above were analyzed the following day after being kept overnight at ambient temperature. The E_E value at the RQL was 95.1%, while that of the working range samples (excluding samples through which humid air had been drawn) was 96.9%. The data are shown in Table B-5. Pre-loading filters with moisture ("wet" designation in the table) did not have an unacceptable effect on E_E.

Table B-5. Extraction efficiency data for the hexamethylene diisocyanate 1-2PP derivative (µg per sample as the underivatized analyte).

level		sample number				
× target concn	µg per sample	1	2	3	4	mean
0.1	0.200	94.1	96.5	91.7	93.2	93.9
0.25	0.520	96.2	96.2	96.2	96.2	96.2
0.5	1.02	96.0	97.8	96.9	97.8	97.1
1.0	2.04	98.6	98.6	99.1	98.2	98.6
1.5	2.99	97.6	99.9	98.3	97.3	98.3
2.0	4.07	98.2	97.1	96.1	98.2	97.4
RQL	0.0370	94.4	97.2	100.0	88.9	95.1
1.0 (wet)	2.04	97.9	98.4	97.9	98.9	98.3
1.0 (dry)[a]	2.09	93.8	96.1	94.8	95.0	94.9
1.0 (wet)[a]	2.09	95.2	94.7	98.7	97.3	96.5

[a] Underivatized hexamethylene diisocyanate spiked onto four replicate coated filters

The stability of sample extracts prepared according to OSHA Method 5002 was examined by retaining the sample solvent extracts for the target concentration samples described immediately above. Two of the four vials were immediately recapped with new septa following the initial analyses, and again following each re-analysis event. The other two vials retained the original punctured septa throughout. All four vials were re-analyzed at 24, 48, and 72 hours after the initial analyses, with all vials remaining in an autosampler tray kept at 8.0 °C. Freshly prepared standards were used for each analysis event, and each septum (whether new or previously used) was punctured one time for each injection. The resulting data are shown in Table B-6.

Table B-6. Extracted sample stability data for the hexamethylene diisocyanate 1-2PP derivative.

	punctured septa replaced recovery (%)		punctured septa retained recovery (%)	
time (days)	1	2	1	2
0	104.6	104.6	105.3	104.1
1	103.0	103.2	104.3	103.5
2	104.9	103.7	104.4	104.0
3	104.7	102.9	104.1	105.4

7 Sampler Capacity

Pre-existing data from OSHA Method 42[1] are presented in this section.

The sampling capacity of a coated filter was tested by performing a sample media analyte retention test. A filter to be spiked was mounted within a cassette in front of another coated filter, with a spacer separating the two filters. Six coated filters were liquid spiked with hexamethylene-diisocyanate 1-2PP derivative nominally at four times the target concentration (calculated to be 0.0798 ppm). Air was drawn through these samplers with a flow rate of 1.0 L/min for

240 min. The relative humidity and temperature were 71% and 21.0 °C. Breakthrough was not observed after sampling for 240 min (corresponding to 240 liters). Data from six coated samplers, as shown in Table B-7, were used to determine the recommended sampling volume of 15 liters for hexamethylene diisocyanate as described in OSHA Method 5002. This volume corresponds to a 15 min sampling period, which is the maximum recommended sampling time regardless of breakthrough.

Table B-7. Retention data for the hexamethylene diisocyanate 1-2PP derivative.

sample no.	air volume (L)	recovery front (%)	recovery back (%)
1	240	103.5	0.0
2	240	103.1	0.0
3	240	102.3	0.0
4	240	102.6	0.0
5	240	102.0	0.0
6	240	102.0	0.0

8 Low Humidity

Pre-existing data from OSHA Method 42[1] are presented in this section.

The effect of low humidity was tested by spiking underivatized hexamethylene diisocyanate onto silanized glass wool placed in a glass tube or syringe directly upstream of a sampling cassette containing a 1-2PP coated filter. The mass of hexamethylene diisocyanate spiked was nominally equivalent to the mass of analyte that would be sampled at seventeen times the target concentration (calculated to be 0.353 ppm) in air for 15 min at a flow rate of 1.0 L/min. Following spiking of the underivatized compound onto the glass wool, dry air (12.0% relative humidity at 21.0 °C) was drawn through each of two samplers thus prepared at a flow rate of 1.0 L/min for 200 min. After immediate analysis, results for the hexamethylene diisocyanate 1-2PP derivative as a percentage of expected recovery were 97.2% and 95.6%.

9 Chemical Interference

The effect of potential chemical sampling interference was tested by spiking underivatized hexamethylene diisocyanate onto silanized glass wool placed in a glass tube or syringe directly upstream of a sampling cassette containing a 1-2PP coated filter. The mass of hexamethylene diisocyanate spiked was nominally equivalent to the mass that would be sampled at the target concentration (calculated to be 0.0195 ppm) in air for 15 min at a flow rate of 1.0 L/min. Underivatized toluene-2,6-diisocyanate and toluene-2,4-diisocyanate (TDI) interferents were also spiked at masses corresponding to sampling these under the same conditions at concentrations of 0.0229 ppm and 0.0229 ppm respectively. Following spiking of the underivatized compounds onto the glass wool, humid air (81.0% relative humidity at 21.0 °C) was drawn through each of three samplers thus prepared via the spiking system at a flow rate of 1.0 L/min for 15 min. After immediate analysis, results for the hexamethylene diisocyanate 1-2PP derivative as a percentage of expected recovery were 99.1%, 100.7%, and 98.0%.

10 Analytical Method Reproducibility

Pre-existing data from OSHA Method 42[1] are presented in this section.

Samples were prepared by spiking five 1-2PP coated filters with the underivatized hexamethylene diisocyanate in such a way that the mass of the analyte that would be sampled at the target concentration in air for 20 min at a sampling rate of 1.0 L/min (calculated to be 0.0265 ppm). Following spiking, 20 L of humidified air (80.0% relative humidity at 21.0 °C) was drawn through each filter in a cassette. The resulting samples were submitted to the OSHA Salt Lake

Technical Center for analysis using the procedures described in OSHA Method 42 after refrigerated (-26.0 °C) storage for 6 days. The analytical results corrected for E_E are provided in Table B-8. No sample result for the hexamethylene diisocyanate derivative fell outside the permissible bounds set by the precision of the overall procedure determined in Section 5 of this appendix.

Table B-8. Reproducibility data for the underivatized hexamethylene diisocyanate.

spiked (μg/sample)	recovered (μg/sample)	recovery (%)	deviation (%)
3.64	3.69	101.4	+1.4
3.64	3.54	97.2	-2.8
3.64	3.72	102.2	+2.2
3.64	3.69	101.4	+1.4
3.64	3.67	100.8	+0.8

11 Effect of Sampling a Low Concentration

A study has not been undertaken to verify the effect of sampling a low concentration of hexamethylene diisocyanate vapor.

12 Estimation of Uncertainty

While systematic biases such as analyte storage loss are examined, and limits are placed on these, an estimation of uncertainty that encompasses both potential random and systematic error was not completed. Instead, the overall standard error of estimate was calculated from the random error inherent to the points about the regression line produced by the ambient storage test described in Section 5, as prescribed by the OSHA validation guidelines in use at the time OSHA Method 5002 was originally validated. See Section 5 of this appendix for details.

13 Controlled Test Atmosphere Procedure

A controlled test atmosphere containing hexamethylene diisocyanate vapor was not generated.

OSHA 5002, Appendix C
Toluene-2,6-diisocyanate

Version:	1.0
OSHA PEL:	None
ACGIH TLV:	0.001 ppm (0.007 mg/m^3) 8-Hour TWA, inhalable fraction and vapor 0.005 ppm (0.035 mg/m^3) 15 Minute STEL, inhalable fraction and vapor
Recommended sampling time and sampling rate:	15 min at 1.0 L/min (15 L)
Reliable quantitation limit:	0.20 ppb (1.4 μg/m^3)
Standard error of estimate:	5.7%
Status:	Fully validated. Method 5002 has been subjected to the established validation procedures of the Method Development Team for sampling and analysis of toluene-2,6-diisocyanate.

March 1989 (OSHA 42)
February 2021 (OSHA 5002)

Donald Burright
Radhakrishnan Ukkiramapandian

1 Introduction

1.1 Methods used by OSHA for Sampling and Analysis Toluene-2,6-Diisocyanate

The specific analyte described in this appendix is toluene-2,6-diisocyanate CAS No. 91-08-7. The methodologies described in this appendix for toluene-2,6-diisocyanate are based on OSHA Method 42.[1] That method requires the collection of samples using a 1-(2-pyridyl)piperazine (1-2PP)-coated glass fiber filter, extraction using 90/10 (v/v) acetonitrile/dimethyl sulfoxide (ACN/DMSO), and analysis by liquid chromatography using a fluorescence detector.

1.2 Changes to the Previously-Used Method

This appendix represents an update of OSHA Method 42[1], which was fully validated at the time it was published based on the validation guidelines in effect at that time. Compared to the previous method used, this method includes new analytical parameters and extraction solvent volume. Data presented from the previously used method are identified by the statement “Pre-existing data from OSHA Method 42[1] are presented in this section”. The changes were made to allow the standardized collection and analysis of toluene-2,6-diisocyanate with other analytes found in Organic Vapor Sampling Group 3 described in OSHA Method 5002.

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[1] Burright, D. Toluene-2,6-diisocyanate (OSHA Method 42), 1989. United States Department of Labor, Occupational Safety & Health Administration Web site. https://www.osha.gov/dts/sltc/methods/organic/org042/org042.html (accessed July 2020).

1.3 Validation Parameters

The procedures used to develop the method validation data are described in Validation Guidelines for Air Sampling Methods Utilizing Chromatographic Analysis.[2] Air concentrations listed in ppm are referenced to 25 °C and 760 Torr. The target concentration for method evaluation was 0.02 ppm for toluene-2,6-diisocyanate.

2 Detection and Quantification

2.1 Detection Limit of the Analytical Procedure (DLAP)

The DLAP is the analyte mass introduced onto the chromatographic column that produces a response greater than 3× the standard error of estimate (DLAP $S_{y/x}$) divided by the slope of the line produced from analyses of ten analytical standards prepared with equally spaced increments of analyte derivative mass. The standards were prepared in such a way that the highest 1-2PP derivative standard concentration would produce a peak approximately 10 times the response of a reagent blank at or near the chromatographic retention time of the analyte derivative. The standards and a reagent blank were analyzed with the recommended analytical parameters described in OSHA Method 5002. The resulting data provided the DLAP $S_{y/x}$ and slope values for DLAP determination. Results obtained for these analyses are listed in Table C-1 and plotted in Figure C-1.

Table C-1. DLAP data for toluene-2,6-diisocyanate 1-2PP derivative (concentration and mass on column as the underivatized analyte).

concentration (ng/mL)	mass on column (pg)	area counts (μV·s)
0.00	0.00	0.00
0.690	2.07	45,080
1.38	4.14	54,860
2.07	6.21	107,100
2.76	8.28	142,300
3.45	10.3	171,300
4.14	12.4	208,000
4.83	14.5	227,500
5.52	16.6	245,500
6.21	18.6	284,300
6.90	20.7	307,300

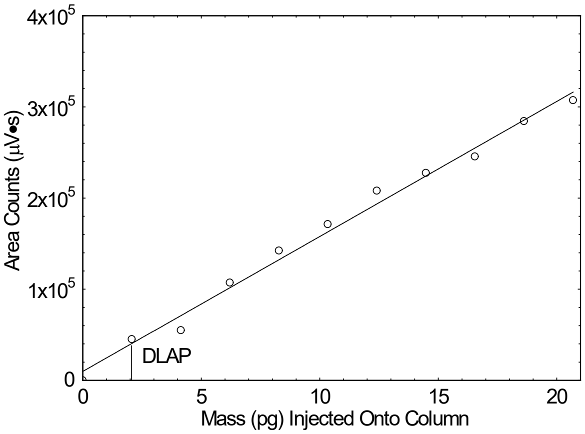

Figure C-1. Plot of data used to determine the DLAP for the toluene-2,6-diisocyanate 1-2PP derivative (as the underivatized analyte, $y = 14{,}806x + 9849$, DLAP $S_{y/x} =$ 10,511, DLAP = 2.13 pg).

2.2 Detection Limit of the Overall Procedure (DLOP) and Reliable Quantitation Limit (RQL)

The DLOP is the analyte mass introduced onto the chromatographic column that produces a response greater than 3× the standard error of estimate (DLOP $S_{y/x}$) divided by the slope of the line produced from analyses of ten samples prepared from coated filters spiked with equally spaced increments of analyte derivative mass. The coated filters were spiked in such a way that the highest 1-2PP derivative mass loading produced a peak approximately 10 times greater than that of a sample blank at or near the chromatographic retention time of the analyte derivative. The RQL is expressed as an air concentration that will provide sufficient analyte mass per sample that produces a response greater than 10× DLOP $S_{y/x}$divided by the slope of the line described above. The spiked samplers and a sample blank were analyzed with the recommended analytical parameters described in OSHA Method 5002.The resulting data provided the DLOP $S_{y/x}$ and slope values for DLOP and RQL determinations. Results obtained from these analyses are listed in

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[2] Eide, M.; Simmons, M.; Hendricks, W. Validation Guidelines for Air Sampling Methods Utilizing Chromatographic Analysis, 2010. United States Department of Labor, Occupational Safety & Health Administration Web site. http://www.osha.gov/dts/sltc/methods/chromguide/chromguide.pdf (accessed July 2020).

Table C-2 and plotted in Figure C-2.

Table C-2. DLOP and RQL data for the toluene-2,6-diisocyanate 1-2PP derivative (mass per sample as the underivatized analyte).

mass per sample (ng/sample)	area counts (μV·s)
0.00	0.00
17.2	315,000
34.5	572,200
51.7	793,300
69.0	1,073,000
86.2	1,343,000
103	1,668,000
121	1,883,000
138	2,163,000
155	2,378,000
172	2,610,000

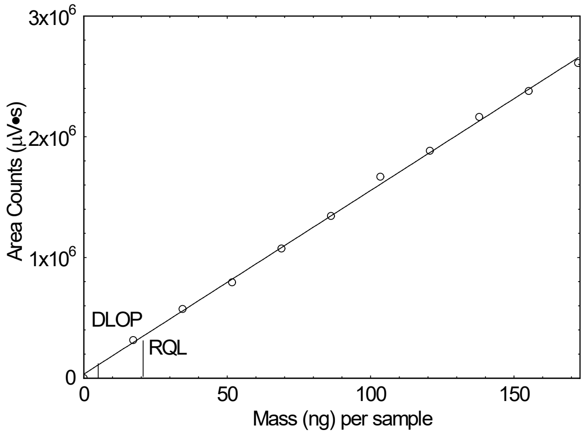

Figure C-2. Plot of data used to determine the DLOP and RQL for the toluene-2,6-diisocyanate 1-2PP derivative (as the underivatized analyte, $y = 15{,}229x + 33{,}400$, DLOP $S_{y/x}$ = 33,070, DLOP = 6.51 ng/sample, RQL = 21.7 ng/sample or 0.203 ppb).

3 Analytical Precision Across the Calibration Range

Fifteen standards for the 1-2PP derivative were analyzed with the recommended analytical parameters described in OSHA Method 5002. These standards ranged from 0.1 to 2.0 times the analyte concentration in solvent that would be obtained from sampling the underivatized analyte for the recommended time at the target concentration. An ordinary least-squares linear regression curve was created by plotting the analyte mass per sample versus the corresponding area count of the analyte derivative peak. The resulting data provided the standard error of estimate (Calibration $S_{y/x}$) value across the calibration range, which provides an indication of the imprecision attributable to the instrumental analysis of the target analyte. Results from these analyses are listed in Table C-3, and plotted in Figure C-3.

Table C-3. Analytical precision data for the toluene-2,6-diisocyanate 1-2PP derivative (concentration as the underivatized analyte).

× target	0.1×	0.5×	1.0×	1.5×	2.0×
concn (μg/sample)	0.217	1.08	2.16	3.16	4.30
area counts X10^4	309.8	1494	2989	4283	5908
	313.8	1487	2957	4271	5877
	310.3	1495	2964	4270	5895

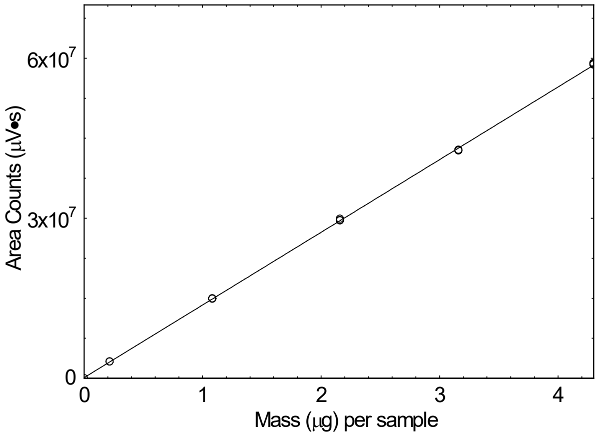

Figure C-3. Plot of data used to determine the precision of the analytical method for the toluene-2,6-diisocyanate 1-2PP derivative (as toluene-2,6-diisocyanate, $y = 13{,}614{,}624x + 156{,}430$, Calibration $S_{y/x}$ = 264,662).

4 Sampler Storage Stability

Storage stability test samples were prepared by spiking the toluene-2,6-diisocyanate 1-2PP derivative onto coated filters. The mass of the toluene-2,6-diisocyanate 1-2PP derivative spiked was stoichiometrically equivalent to the mass of the underivatized analyte that would be sampled at the target concentration (calculated to be 0.0227 ppm) in air for 15 min at a flow rate of 1.0 L/min. Humid air (81.0% relative humidity at 22.0 °C) was then drawn through each filter following the recommended sampling parameters published in OSHA Method 5002. Eighteen such storage samples were prepared and three of these were analyzed on the same day that samples were created. The remaining fifteen samples were stored in a closed drawer at ambient temperature (about 22.0 °C). Three samples were selected and analyzed from those remaining at 3-4 day intervals. The results of these analyses (uncorrected for extraction efficiency) are provided in Table C-4 and in Figure C-4.

The recovery of the toluene-2,6-diisocyanate 1-2PP derivative calculated from the regression line generated for the 18-day ambient storage test was 100.2%.

Table C-4. Sampler storage stability data for the toluene-2,6-diisocyanate 1-2PP derivative.

time (days)	ambient storage recovery (%)		
0	94.2	98.4	95.1
3	94.9	93.8	94.6
7	102.7	96.9	99.2
10	93.6	94.4	94.3
14	102.1	97.9	99.0
18	102.4	101.8	99.0

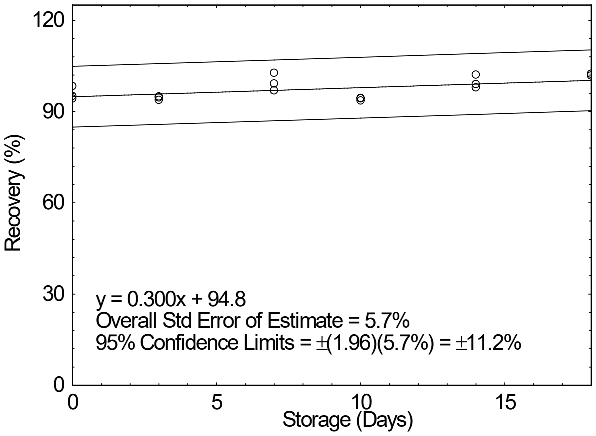

Figure C-4. Plot of ambient storage stability data for the toluene-2,6-diisocyanate 1-2PP derivative.

5 Precision of the Overall Procedure

The overall standard error of estimate obtained from the ambient storage test analyses described in Section 4 and sampling pump variability were used to determine the precision of the overall procedure, where all aspects of sampling and analysis (sampling, filter handling and solvent extraction, and instrumental analysis) are considered. This value was obtained by taking the square root of the squared ambient storage stability standard error of estimate (Storage $S^2_{y/x}$) added to the squared sampling pump variability value (V^2_{SP}). The resulting precision of the overall procedure at the 95% confidence level for the ambient 18-day storage test (at the target concentration) for the toluene-2,6-diisocyanate 1-2PP derivative was determined to be ±11.2% based on the observed ambient Storage $S_{y/x}$ value of 5.7% and V_{SP} value of 5.0%.

6 Recovery and Stability of Prepared Samples

Quantitative extraction is affected by the extraction solvent, the sampling medium, and the technique used to extract samples. The data presented demonstrate validity for the extraction solvent, sampling medium and extraction technique described in OSHA Method 5002. If other combinations of these are to be used, testing must be completed to satisfy the requirements found in current OSHA sampling and analysis method validation guidelines. Acceptable testing results must be documented.

A value for extraction efficiency (E_E) was determined by spiking the toluene-2,6-diisocyanate 1-2PP derivative onto four 1-2PP coated filters across a range of analyte derivative mass values that would be obtained from sampling the underivatized analyte at 0.1 to 2 times the target concentration value for 15 min. Four filters were also spiked in this fashion at the target concentration after drawing humid air (80.0% relative humidity at 21.0 °C) through these filters at 1.0 L/min for 15 min. All of the samples described above were analyzed the following day after being kept overnight at ambient temperature. The E_E value at the RQL was 98.7%, while that of the working range samples (excluding samples through which humid air had been drawn) was 97.5%. The data are shown in Table C-5. Pre-loading filters with moisture ("wet" designation in the table) did not have an unacceptable effect on E_E.

Table C-5. Extraction efficiency data for the toluene-2,6-diisocyanate 1-2PP derivative (µg per sample as the underivatized analyte).

level		sample number				
× target concn	µg per sample	1	2	3	4	mean
0.1	0.220	96.7	97.2	94.8	94.3	95.8
0.25	0.550	97.5	95.5	97.5	95.5	96.5
0.5	1.09	98.5	97.5	98.5	98.5	98.2
1.0	2.17	99.2	97.8	98.8	98.3	98.5
1.5	3.19	99.6	98.9	99.6	98.0	99.0
2.0	4.34	97.4	96.7	96.1	98.6	97.2
RQL	0.0200	100.0	100.0	94.7	100.0	98.7
1.0 (wet)	2.17	98.3	98.7	99.2	98.3	98.6
1.0 (dry)[a]	2.45	99.3	100.4	97.0	100.7	99.4
1.0 (wet)[a]	2.45	98.5	100.4	96.2	92.8	97.0

[a] Underivatized toluene-2,6-diisocyanate spiked onto four replicate coated filters

The stability of sample extracts prepared according to OSHA Method 5002 was examined by retaining the sample solvent extracts for the target concentration samples described immediately above. Two of the four vials were immediately recapped with new septa following the initial analyses, and again following each re-analysis event. The other two vials retained the original punctured septa throughout. All four vials were re-analyzed at 24, 48, and 72 hours after the initial analyses, with all vials remaining in an autosampler tray kept at 8 °C. Freshly prepared standards were used for each re-analysis event, and each septum (whether new or previously used) was punctured one time for each injection. The resulting data are shown in Table C-6.

Table C-6. Extracted sample stability data for the toluene-2,6-diisocyanate 1-2PP derivative.

	punctured septa replaced recovery (%)		punctured septa retained recovery (%)	
time (days)	1	2	1	2
0	98.6	97.4	98.3	97.6
1	97.7	96.2	97.9	96.2
2	97.9	96.9	98.9	97.0
3	97.8	96.6	97.3	98.8

7 Sampler Capacity

Pre-existing data from OSHA Method 42[1] are presented in this section.

The sampling capacity of a coated filter was tested by performing a sample media analyte retention test. A filter to be spiked was mounted within a cassette in front of another coated filter, with a spacer separating the two filters. Six coated filters were liquid spiked with toluene-2,6-diisocyanate 1-2PP derivative nominally at four times the target concentration (calculated to be 0.0788 ppm). Air was drawn through these samplers with a flow rate of 1.0 L/min for

240 min. The relative humidity and temperature were 71% and 21.0 °C. Breakthrough was not observed after sampling for 240 min (corresponding to 240 liters). Data from six coated samplers, as shown in Table C-7, were used to determine the recommended sampling volume of 15 liters for toluene-2,6-diisocyanate as described in OSHA Method 5002. This volume corresponds to a 15 min sampling period, which is the maximum recommended sampling time regardless of breakthrough.

Table C-7. Retention data for the toluene-2,6-diisocyanate 1-2PP derivative.

sample no.	air volume (L)	recovery front (%)	recovery back (%)
1	240	103.1	0.0
2	240	100.3	0.0
3	240	102.7	0.0
4	240	98.7	0.0
5	240	97.1	0.0
6	240	96.7	0.0

8 Low Humidity

Pre-existing data from OSHA Method 42[1] are presented in this section.

The effect of low humidity was tested by spiking underivatized toluene-2,6-diisocyanate onto silanized glass wool placed in a glass tube or syringe directly upstream of a sampling cassette containing a 1-2PP coated filter. The mass of toluene-2,6-diisocyanate spiked was nominally equivalent to the mass that would be sampled at ten times the target concentration (calculated to be 0.261 ppm) in air for 15 min at a flow rate of 1.0 L/min. Following spiking of the underivatized compound onto the glass wool, dry air (12.0% relative humidity at 21.0 °C) was drawn through each of two samplers thus prepared via the spiking system at a flow rate 1.0 L/min for 200 min. After immediate analysis, results for the toluene-2,6-diisocyanate 1-2PP derivative as a percentage of expected recovery were 96.9% and 95.6%.

9 Chemical Interference

The effect of potential chemical sampling interference was tested by spiking underivatized toluene-2,6-diisocyanate onto silanized glass wool placed in a glass tube or syringe directly upstream of a sampling cassette containing a 1-2PP coated filter The mass of toluene-2,6-diisocyanate spiked was nominally equivalent to the mass that would be sampled at the target concentration (calculated to be 0.0229 ppm) in air for 15 min at a flow rate of 1.0 L/min. Underivatized toluene-2,4-diisocyanate (TDI) and hexamethylene diisocyanate interferents were also spiked at masses corresponding to sampling these under the same conditions at concentrations of 0.0229 ppm and 0.0195 ppm respectively. Following spiking of the underivatized compounds onto the glass wool, humid air (81.0% relative humidity at 21.0 °C) was drawn through each of three samplers thus prepared via the spiking system at a flow rate of 1.0 L/min for 15 min. After immediate analysis, results for the toluene-2,6-diisocyanate 1-2PP derivative as a percentage of expected recovery were 93.2%, 91.4%, and 90.8%.

10 Analytical Method Reproducibility

Pre-existing data from OSHA Method 42[1] are presented in this section.

Samples were prepared by spiking five 1-2PP coated filters with the underivatized toluene-2,6-diisocyanate in such a way that the mass of the analyte that would be sampled at the target concentration in air for 20 min at a sampling rate of 1.0 L/min (calculated to be 0.0196 ppm). Following this, 20 L of humidified air (80.0% relative humidity at 21.0 °C) was drawn through each filter in a cassette. The resulting samples were submitted to the OSHA Salt Lake Technical Center for analysis using the procedures described in OSHA Method 42 after refrigerated (-26.0 °C) storage for 6 days. The analytical results corrected for E_E are provided in Table C-8. No sample result for the toluene-2,6-diisocyanate derivative fell outside the permissible bounds set by the precision of the overall procedure determined in Section 5 of this appendix.

Table C-8. Reproducibility data for the underivatized toluene-2,6-diisocyanate.

spiked (µg/sample)	recovered (µg/sample)	recovery (%)	deviation (%)
2.79	2.86	102.5	+2.5
2.79	2.76	98.9	-1.1
2.79	2.87	102.9	+2.9
2.79	2.86	102.5	+2.5
2.79	2.83	101.4	+1.4

11 Effect of Sampling a Low Concentration

A study has not been undertaken to verify the effect of sampling a low concentration of toluene-2,6-diisocyanate vapor.

12 Estimation of Uncertainty

While systematic biases such as analyte storage loss are examined, and limits are placed on these, an estimation of uncertainty that encompasses both potential random and systematic error was not completed. Instead, the overall standard error of estimate was calculated from the random error inherent to the points about the regression line produced by the ambient storage test described in Section 5, as prescribed by the OSHA validation guidelines in use at the time OSHA Method 5002 was originally validated. See Section 5 of this appendix for details.

13 Controlled Test Atmosphere Procedure

A controlled test atmosphere containing toluene-2,6-diisocyanate vapor was not generated.

OSHA 5002, Appendix D
Methylene Bisphenyl Isocyanate (MDI)

Version:	1.0
OSHA PEL:	0.02 ppm (0.2 mg/m^3) Ceiling, General Industry, Construction, Shipyard
ACGIH TLV:	0.005 ppm (0.051 mg/m^3) 8-Hour TWA
Recommended sampling time and sampling rate:	15 min at 1.0 L/min (15 L)
Reliable quantitation limit:	0.25 ppb (2.6 μg/m^3)
Standard error of estimate:	6.2%
Status:	Fully validated. Method 5002 has been subjected to the established validation procedures of the Method Development Team for sampling and analysis of methylene bisphenyl isocyanate (MDI).

March 1989 (OSHA 47)
February 2021 (OSHA 5002)

Donald Burright
Radhakrishnan Ukkiramapandian

1 Introduction

1.1 Previous Methods used by OSHA for Sampling and Analysis of Methylene Bisphenyl Isocyanate (MDI)

The specific analyte described in this appendix is methylene bisphenyl isocyanate (MDI) CAS No. 101-68-8. The methodologies described in this appendix for methylene bisphenyl isocyanate (MDI) are based on OSHA Method 47.[1] That method requires the collection of samples using a 1-(2-pyridyl)piperazine (1-2PP)-coated glass fiber filter, extraction using 90/10 (v/v) acetonitrile/dimethyl sulfoxide (ACN/DMSO), and analysis by liquid chromatography using a fluorescence detector.

1.2 Changes to the Previously-Used Method

This appendix represents an update of OSHA Method 47[1], which was fully validated at the time it was published based on the validation guidelines in effect at that time. Compared to the previous method used, this method includes new analytical parameters and extraction solvent volume. Data presented from the previously used method are identified by the statement “Pre-existing data from OSHA Method 47[1] are presented in this section”. The changes were made to allow the standardized collection and analysis of methylene bisphenyl isocyanate (MDI) with other analytes found in Organic Vapor Sampling Group 3, described in OSHA Method 5002.

1.3 Validation Parameters

The procedures used to develop the method validation data are described in Validation Guidelines for Air Sampling Methods Utilizing Chromatographic Analysis.[2] Air concentrations listed in ppm are referenced to 25 °C and 760 Torr.

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[1] Burright, D. Methylene bisphenyl isocyanate (MDI) (OSHA Method 47), 1989. United States Department of Labor, Occupational Safety & Health Administration Web site. https://www.osha.gov/dts/sltc/methods/organic/org047/org047.html (accessed July 2020).

[2] Eide, M.; Simmons, M.; Hendricks, W. Validation Guidelines for Air Sampling Methods Utilizing Chromatographic Analysis, 2010. United States Department of Labor, Occupational Safety & Health Administration Web site. http://www.osha.gov/dts/sltc/methods/chromguide/chromguide.pdf (accessed July 2020).

The target concentration for method evaluation was the OSHA ceiling permissible exposure limit for methylene bisphenyl isocyanate (MDI).

2 Detection and Quantification

2.1 Detection Limit of the Analytical Procedure (DLAP)

The DLAP is the analyte mass introduced onto the chromatographic column that produces a response greater than 3× the standard error of estimate (DLAP $S_{y/x}$) divided by the slope of the line produced from analyses of ten analytical standards prepared with equally spaced increments of analyte derivative mass. The standards were prepared in such a way that the highest 1-2PP derivative standard concentration would produce a peak approximately 10 times the response of a reagent blank at or near the chromatographic retention time of the analyte derivative. The standards and a reagent blank were analyzed with the recommended analytical parameters described in OSHA Method 5002. The resulting data provided the DLAP $S_{y/x}$ and slope values for DLAP determination. Results obtained for these analyses are listed in Table D-1 and plotted in Figure D-1.

Table D-1. DLAP data for the methylene bisphenyl isocyanate (MDI) 1-2PP derivative (concentration and mass on column as the underivatized analyte).

concentration (ng/mL)	mass on column (pg)	area counts (µV·s)
0.00	0.00	0.00
0.855	2.57	12,200
1.71	5.13	39,290
2.57	7.70	98,500
3.42	10.3	122,300
4.28	12.8	151,200
5.13	15.4	208,300
5.99	18.0	259,200
6.84	20.5	294,100
7.70	23.1	324,000
8.55	25.7	350,300

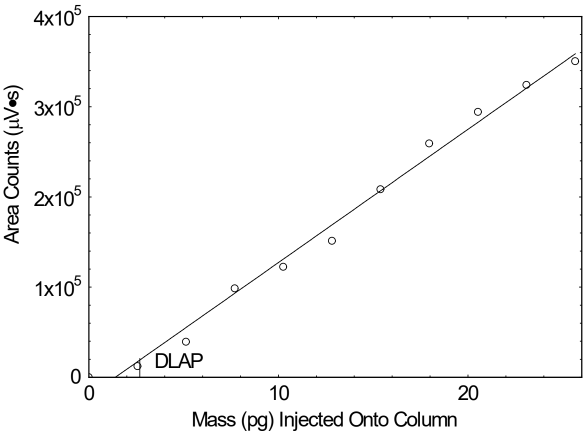

Figure D-1. Plot of data used to determine the DLAP for the methylene bisphenyl isocyanate (MDI) 1-2PP derivative (as the underivatized analyte, $y = 14{,}767x - 20{,}515$, DLAP $S_{y/x}$ = 13,083, DLAP = 2.66 pg).

2.2 Detection Limit of the Overall Procedure (DLOP) and Reliable Quantitation Limit (RQL)

The DLOP is the analyte mass introduced onto the chromatographic column that produces a response greater than 3× the standard error of estimate (DLOP $S_{y/x}$) divided by the slope of the line produced from analyses of ten samples prepared from coated filters spiked with equally spaced increments of analyte derivative mass. The coated filters were spiked in such a way that the highest 1-2PP derivative mass loading produced a peak approximately 10 times greater than that of a sample blank at or near the chromatographic retention time of the analyte derivative. The RQL is expressed as an air concentration that will provide sufficient analyte mass per sample that produces a response greater than 10× DLOP $S_{y/x}$divided by the slope of the line described above. The spiked samplers and a sample blank were analyzed with the recommended analytical parameters described in OSHA Method 5002.The resulting data provided the DLOP $S_{y/x}$ and slope values for DLOP and RQL determinations. Results obtained from these analyses are listed in Table D-2 and plotted in Figure D-2.

Table D-2. DLOP and RQL data for the methylene bisphenyl isocyanate (MDI) 1-2PP derivative (mass per sample as the underivatized analyte).

mass per sample (ng/sample)	area counts (µV·s)
0.00	0.00
21.4	359,300
42.8	567,400
64.1	857,000
85.5	1,050,000
107	1,271,000
128	1,626,000
150	1,810,000
171	2,007,000
192	2,273,000
214	2,534,000

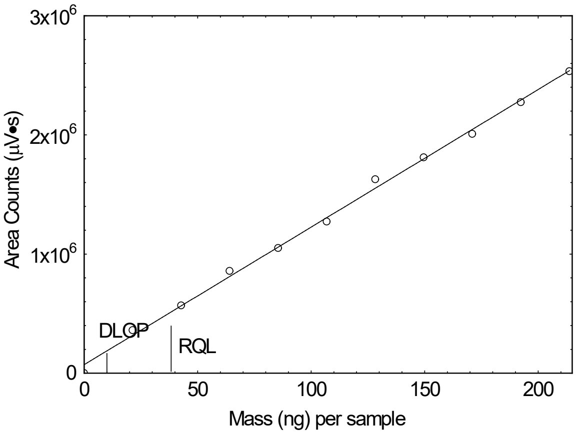

Figure D-2. Plot of data used to determine the DLOP and RQL for the methylene bisphenyl isocyanate (MDI) 1-2PP derivative (as the underivatized analyte, $y = 11{,}536x + 71{,}871$, DLOP $S_{y/x}$ = 44,620, DLOP = 11.6 ng/sample, RQL = 38.7 ng/sample or 0.252 ppb).

3 Analytical Precision Across the Calibration Range

Fifteen standards for the 1-2PP derivative were analyzed with the recommended analytical parameters described in OSHA Method 5002. These standards ranged from 0.1 to 2.0 times the analyte concentration in solvent that would be obtained from sampling the underivatized analyte for the recommended time at the target concentration. An ordinary least-squares linear regression curve was created by plotting the analyte mass per sample versus the corresponding area count of the analyte derivative peak. The resulting data provided the standard error of estimate (Calibration $S_{y/x}$) value across the calibration range, which provides an indication of the imprecision attributable to the instrumental analysis of the target analyte. Results from these analyses are listed in Table D-3, and plotted in Figure D-3.

Table D-3. Analytical precision data for the methylene bisphenyl isocyanate (MDI) 1-2PP derivative (concentration as the underivatized analyte).

× target	0.1×	0.5×	1.0×	1.5×	2.0×
concn (µg/sample)	0.349	1.74	3.47	5.08	6.91
area counts x 10^4 (µV·s)	386.7	1891	3800	5427	7491
	387.3	1891	3782	5443	7534
	385.9	1906	3751	5443	7466

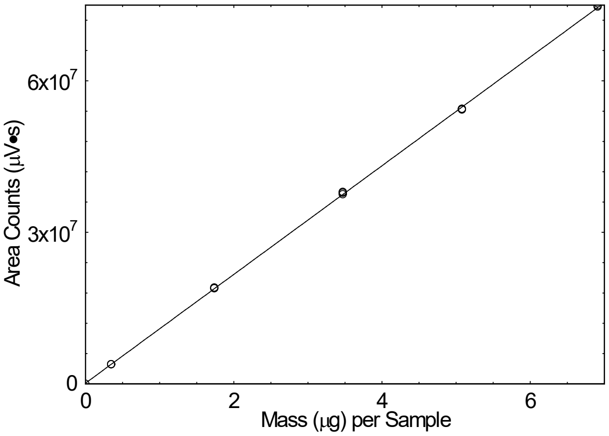

Figure D-3. Plot of data used to determine the precision of the analytical method for the methylene bisphenyl isocyanate (MDI) 1-2PP derivative (as the underivatized analyte, $y = 10{,}791{,}947x - 112{,}358$, Calibration $S_{y/x}$ = 364,568).

4 Sampler Storage Stability

Storage stability test samples were prepared by spiking the methylene bisphenyl isocyanate (MDI) 1-2PP derivative onto coated filters. The mass of the methylene bisphenyl isocyanate (MDI) 1-2PP derivative spiked was stoichiometrically equivalent to the mass of the underivatized analyte that would be sampled at the target concentration (calculated to be 0.0287 ppm) in air for 15 min at a flow rate of 1.0 L/min. Humid air (81.0% relative humidity at 22.0 °C) was then drawn through each filter following the recommended sampling parameters published in OSHA Method 5002. Eighteen such storage samples were prepared and three of these were analyzed on the same day that samples were created. The remaining fifteen samples were stored in a closed drawer at ambient temperature (about 22.0 °C). Three samples were selected and analyzed from those remaining at 3-4 day intervals. The results of these analyses (uncorrected for extraction efficiency) are provided in Table D-4 and in Figure D-4.

The recovery of the methylene bisphenyl isocyanate (MDI) 1-2PP derivative calculated from the regression line generated for the 18-day ambient storage test was 99.9%.

Table D-4. Sampler storage stability data for the methylene bisphenyl isocyanate (MDI) 1-2PP derivative.

time (days)	ambient storage recovery (%)		
0	97.5	103.9	99.0
3	94.9	95.2	95.6
7	104.9	98.2	99.7
10	92.8	96.2	96.2
14	101.3	96.9	102.2
18	104.2	101.8	97.1

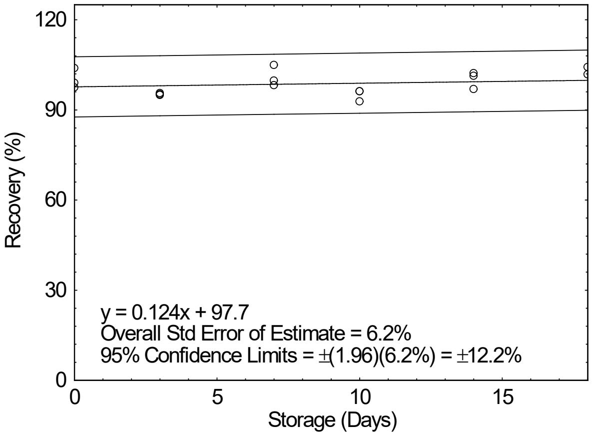

Figure D-4. Plot of ambient storage stability data for the methylene bisphenyl isocyanate (MDI) 1-2PP derivative.

5 Precision of the Overall Procedure

The overall standard error of estimate obtained from the ambient storage test analyses described in Section 4 and sampling pump variability were used to determine the precision of the overall procedure, where all aspects of sampling and analysis (sampling, filter handling and solvent extraction, and instrumental analysis) are considered. This value was obtained by taking the square root of the squared ambient storage stability standard error of estimate (Storage $S_{y/x}^2$) added to the squared sampling pump variability value (V_{SP}^2). The resulting precision of the overall procedure at the 95% confidence level for the ambient 18-day storage test (at the target concentration) for the methylene bisphenyl isocyanate (MDI) 1-2PP derivative was determined to be ±12.2% based on the observed ambient Storage $S_{y/x}$ value of 6.2% and V_{SP} value of 5.0%.

6 Recovery and Stability of Prepared Samples

Quantitative extraction is affected by the extraction solvent, the sampling medium, and the technique used to extract samples. The data presented demonstrate validity for the extraction solvent, sampling medium and extraction technique described in OSHA Method 5002. If other combinations of these are to be used, testing must be completed to satisfy the requirements found in current OSHA sampling and analysis method validation guidelines. Acceptable testing results must be documented.

A value for extraction efficiency (E_E) was determined by spiking the methylene bisphenyl isocyanate (MDI) 1-2PP derivative onto four 1-2PP coated filters across a range of analyte derivative mass values that would be obtained from sampling the underivatized analyte at 0.1 to 2 times the target concentration value for 15 min. Four filters were also spiked in this fashion at the target concentration after drawing humid air (80.0% relative humidity at 21.0 °C) through these filters at 1.0 L/min for 15 min. All of the samples described above were analyzed the following day after being kept overnight at ambient temperature. The E_E value at the RQL was 105.0%, while that of the working range samples (excluding samples through which humid air had been drawn) was 99.1%. The data are shown in Table D-5. Pre-loading filters with moisture ("wet" designation in the table) did not have an unacceptable effect on E_E.

Table D-5. Extraction efficiency data for the methylene bisphenyl isocyanate (MDI) 1-2PP derivative (µg per sample as the underivatized analyte).

level		sample number				
× target concn	µg per sample	1	2	3	4	mean
0.1	0.350	103.3	101.9	99.3	101.3	101.4
0.25	0.880	97.8	96.7	96.7	95.6	96.7
0.5	1.75	99.6	99.6	100.7	99.6	99.9
1.0	3.49	99.8	99.5	100.1	99.5	99.8
1.5	5.12	99.7	99.9	99.7	98.7	99.5
2.0	6.98	97.9	97.1	96.2	98.4	97.4
RQL	0.0330	110.0	116.7	96.7	96.7	105.0
1.0 (wet)	3.49	98.8	99.3	99.6	98.8	99.1
1.0 (dry)[a]	3.20	102.6	98.3	100.8	102.2	101.0
1.0 (wet)[a]	3.20	97.3	96.4	99.9	95.0	97.2

[a] Underivatized methylene bisphenyl isocyanate (MDI) spiked onto four replicate coated filters

The stability of sample extracts prepared according to OSHA Method 5002 was examined by retaining the sample solvent extracts for the target concentration samples described immediately above. Two of the four vials were immediately recapped with new septa following the initial analyses, and again following each re-analysis event. The other two vials retained the original punctured septa throughout. All four vials were re-analyzed at 24, 48, and 72 hours after the initial analyses, with all vials remaining in an autosampler tray kept at 8.0 °C. Freshly prepared standards were used for each re-analysis event, and each septum (whether new or previously used) was punctured one time for each injection. The resulting data are shown in Table D-6.

Table D-6. Extracted sample stability data for the methylene bisphenyl isocyanate (MDI) 1-2PP derivative.

	punctured septa replaced recovery (%)		punctured septa retained recovery (%)	
time (days)	1	2	1	2
0	104.1	103.7	104.2	103.6
1	102.5	101.7	102.8	102.3
2	103.9	103.7	103.9	102.6
3	103.2	102.0	103.4	105.1

7 Sampler Capacity

Pre-existing data from OSHA Method 47[1] are presented in this section.

The sampling capacity of a coated filter was tested by performing a sample media analyte retention test. Six coated filters to be spiked were mounted within a cassette were spiked with methylene bisphenyl isocyanate (MDI) 1-2PP derivative nominally the target concentration (calculated to be 0.0280 ppm). Air was drawn through these samplers with a flow rate of 1.0 L/min for 20 min. The relative humidity and temperature were 80% and 21.0 °C. Data from six coated samplers, as shown in Table D-7, were used to determine the recommended sampling volume of 15 liters for methylene bisphenyl isocyanate (MDI) as described in OSHA Method 5002. This volume corresponds to a 15 min sampling period, which is the maximum recommended sampling time regardless of breakthrough.

Table D-7. Retention data for the methylene bisphenyl isocyanate (MDI) 1-2PP derivative.

sample no.	air volume (L)	recovery front (%)
1	20	95.7
2	20	96.8
3	20	97.2
4	20	98.4
5	20	98.8
6	20	97.5

8 Low Humidity

A study has not been undertaken to verify that sampling under low humidity conditions for methylene bisphenyl isocyanate (MDI) at the target concentration does not produce anomalous results.

9 Chemical Interference

The effect of potential chemical sampling interference was tested by spiking 1-2PP coated filters with the methylene bisphenyl isocyanate (MDI) 1-2PP derivative in such a way that the mass of the derivative spiked was stoichiometrically equivalent to the mass of underivatized analyte that would be sampled at the target concentration (calculated to be 0.0287 ppm) in air for 15 min at a sampling rate of 1.0 L/min. Toluene-2,4-diisocyanate (TDI), toluene-2,6-diisocyanate, and hexamethylene diisocyanate 1-2PP derivatives were also spiked at masses corresponding to sampling these as underivatized interferents under the same conditions at concentrations of 0.0210 ppm, 0.0220 ppm, and 0.0220 ppm respectively. Following this, humid air (81.0% relative humidity at 22.0 °C) was drawn through each filter in a cassette at 1.0 L/min for 15 min. After immediate analysis, results for the methylene bisphenyl isocyanate (MDI) 1-2PP derivative as a percentage of expected recovery were 97.5%, 103.9%, and 99.0%.

10 Analytical Method Reproducibility

Pre-existing data from OSHA Method 47[1] are presented in this section.

Samples were prepared by spiking five 1-2PP coated filters with the methylene bisphenyl isocyanate (MDI) 1-2PP derivative in such a way that the mass of the derivative was approximately stoichiometrically equivalent to the mass of underivatized analyte that would be sampled at the target concentration in air for 15 min at a sampling rate of 1.0 L/min (calculated to be 0.0192 ppm). Following this, 15 L of humidified air (80.0% relative humidity at 21.0 °C) was drawn through each filter in a cassette. The resulting samples were submitted to the OSHA Salt Lake Technical Center for analysis using the procedures described in OSHA Method 47 after ambient (22.0 °C) storage for 6 days. The analytical results corrected for E_E are provided in Table D-8. No sample result for the methylene bisphenyl isocyanate (MDI) derivative fell outside the permissible bounds set by the precision of the overall procedure determined in Section 5 of this appendix.

Table D-8. Reproducibility data for the methylene bisphenyl isocyanate (MDI) 1-2PP derivative (spiked and recovered μg/sample as the underivatized analyte).

spiked (μg/sample)	recovered (μg/sample)	recovery (%)	deviation (%)
2.94	3.10	105.4	+5.4
2.94	3.13	106.5	+6.5
2.94	3.17	107.8	+7.8
2.94	3.28	111.6	+11.6
2.94	3.19	108.5	+8.5
2.94	2.91	99.0	-1.0

11 Effect of Sampling a Low concentration

A study has not been undertaken to verify the effect of sampling a low concentration of methylene bisphenyl isocyanate (MDI) vapor.

12 Estimation of Uncertainty

While systematic biases such as analyte storage loss are examined, and limits are placed on these, an estimation of uncertainty that encompasses both potential random and systematic error was not completed. Instead, the overall standard error of estimate was calculated from the random error inherent to the points about the regression line produced by the ambient storage test described in Section 5, as prescribed by the OSHA validation guidelines in use at the time OSHA Method 5002 was originally validated. See Section 5 of this appendix for details.

13 Controlled Test Atmosphere Procedure

A controlled test atmosphere containing methylene bisphenyl isocyanate (MDI) vapor was not generated.

OSHA 5002, Appendix E
1,6-Hexamethylene Diisocyanate Homopolymer

Version:	1.0
OSHA PEL:	None
ACGIH TLV:	None
Recommended sampling time and sampling rate:	15 min at 1.0 L/min (15 L)
Reliable quantitation limit:	0.031 mg/m^3
Standard error of estimate:	5.1%
Status:	Fully validated. Method 5002 has been subjected to the established validation procedures of the Method Development Team for sampling and analysis of 1,6-hexamethylene diisocyanate homopolymer.

June 2003 (OSHA PV2125)
February 2021 (OSHA 5002)

Yogi Shah
Radhakrishnan Ukkiramapandian

1 Introduction

1.1 Previous Methods used by OSHA for Sampling and Analysis of 1,6-Hexamethylene Diisocyanate Homopolymer

The specific analyte described in this appendix is 1,6-hexamethylene diisocyanate homopolymer CAS No. 28182-81-2. The methodologies described in this appendix for 1,6-hexamethylene diisocyanate homopolymer are based on OSHA Method PV2125.[1] That method requires the collection of samples using a 1-(2-pyridyl)piperazine (1-2PP)-coated glass fiber filter, extraction using 90/10 (v/v) acetonitrile/dimethyl sulfoxide (ACN/DMSO), and analysis by liquid chromatography using a fluorescence detector.

1.2 Changes to the Previously-Used Method

This appendix represents an update of OSHA Method PV2125[1], which was partially validated at the time it was published based on the validation guidelines in effect at that time. Compared to the previous method used, this method includes new analysis parameters and sample preparation. The data found in all subsequent sections of this appendix are new. The changes were made to allow the standardized collection and analysis of 1,6-hexamethylene diisocyanate homopolymer with other analytes found in Organic Vapor Sampling Group 3 described in OSHA Method 5002. While the target analyte has no appreciable vapor pressure, the reactivity of its isocyanate functional groups with 1-2PP, and the ability for Method 5002 liquid chromatography methods to analyze the resulting derivatives make this method suitable for analysis of 1,6-hexamethylene diisocyanate homopolymer aerosol components.

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[1] Shah, Y. 1,6-hexamethylene diisocyanate homopolymer (OSHA Method PV2125), 2003. United States Department of Labor, Occupational Safety & Health Administration Web site.https://www.osha.gov/dts/sltc/methods/partial/pv2125/pv2125.html (accessed July 2020).

1.3 Validation Parameters

The procedures used to develop the method validation data are described in Validation Guidelines for Air Sampling Methods Utilizing Chromatographic Analysis.[2] Air concentrations listed in ppm are referenced to 25 °C and 760 Torr. The target concentration for method evaluation was 0.50 mg/m^3 for 1,6-hexamethylene diisocyanate homopolymer.

2 Detection and Quantification

2.1 Detection Limit of the Analytical Procedure (DLAP)

The DLAP is the analyte mass introduced onto the chromatographic column that produces a response greater than 3× the standard error of estimate (DLAP $S_{y/x}$) divided by the slope of the line produced from analyses of ten analytical standards prepared with equally spaced increments of analyte derivative mass. The standards were prepared in such a way that the highest 1-2PP derivative standard concentration would produce a peak approximately 10 times the response of a reagent blank at or near the chromatographic retention time of the analyte derivative. The standards and a reagent blank were analyzed with the recommended analytical parameters described in OSHA Method 5002. The resulting data provided the DLAP $S_{y/x}$ and slope values for DLAP determination. Results obtained for these analyses are listed in Table E-1 and plotted in Figure E-1.

Table E-1. DLAP data for the 1,6-hexamethylene diisocyanate homopolymer 1-2PP derivative (concentration and mass on column as the underivatized analyte).

concentration (ng/mL)	mass on column (pg)	area counts (µV·s)
0.00	0.00	0.00
19.8	59.4	286,900
39.5	119	456,800
59.3	178	594,500
79.1	237	748,200
98.8	296	816,100
119	357	941,300
138	414	1,182,000
158	474	1,197,000
178	534	1,422,000
198	594	1,667,000

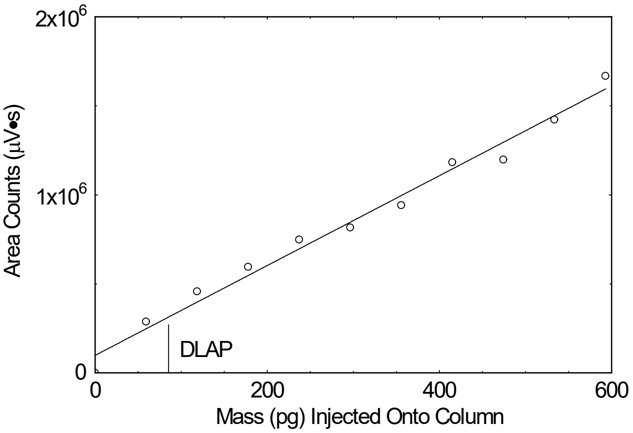

Figure E-1. Plot of data used to determine the DLAP for the 1,6-hexamethylene diisocyanate homopolymer 1-2PP derivative (as the underivatized analyte, $y = 2523x + 98{,}208$, DLAP $S_{y/x}$ = 66,743, DLAP = 79.4 pg).

2.2 Detection Limit of the Overall Procedure (DLOP) and Reliable Quantitation Limit (RQL)

The DLOP is the analyte mass introduced onto the chromatographic column that produces a response greater than 3× the standard error of estimate (DLOP $S_{y/x}$) divided by the slope of the line produced from analyses of ten samples prepared from coated filters spiked with equally spaced increments of analyte derivative mass. The coated filters were spiked in such a way that the highest 1-2PP derivative mass loading produced a peak approximately 10 times greater than that of a sample blank at or near the chromatographic retention time of the analyte derivative. The RQL is expressed as an air concentration that will provide sufficient analyte mass per sample that produces a response greater than 10× DLOP $S_{y/x}$ divided by the slope of the line described above. The spiked samplers and a sample blank were analyzed with the recommended analytical parameters described in OSHA Method 5002.The resulting data provided the DLOP $S_{y/x}$ and slope values for DLOP and RQL determinations. Results obtained from these analyses are listed in

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[2] Eide, M.; Simmons, M.; Hendricks, W. Validation Guidelines for Air Sampling Methods Utilizing Chromatographic Analysis, 2010. United States Department of Labor, Occupational Safety & Health Administration Web site. http://www.osha.gov/dts/sltc/methods/chromguide/chromguide.pdf (accessed July 2020).

Table E-2 and plotted in Figure E-2.

Table E-2. DLOP and RQL data for the 1,6-hexamethylene diisocyanate homopolymer 1-2PP derivative (mass per sample as the underivatized analyte).

mass per sample (µg/sample)	area counts (µV·s)
0.00	138,900
0.395	1,139,000
0.791	1,763,000
1.19	2,491,000
1.58	3,280,000
1.98	3,989,000
2.37	4,745,000
2.77	5,430,000
3.16	6,092,000
3.56	6,741,000
3.95	7,544,000

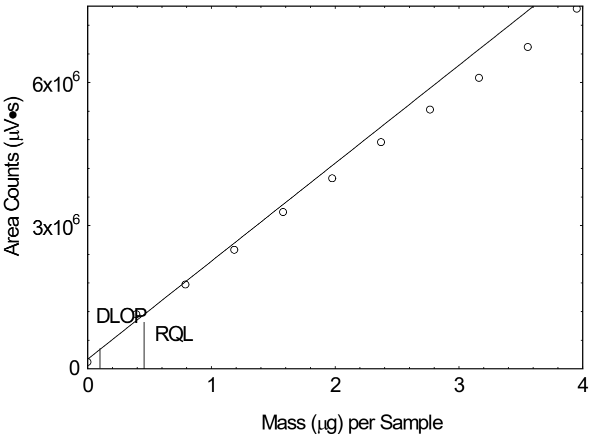

Figure E-2. Plot of data used to determine the DLOP and RQL for the 1,6-hexamethylene diisocyanate homopolymer 1-2PP derivative (as the underivatized analyte, $y = 1{,}834{,}082x + 315{,}559$, DLOP $S_{y/x}$ = 85,763, DLOP = 0.140 µg/sample, RQL = 0.468 µg/sample or 31.2 µg/m^3).

3 Analytical Precision Across the Calibration Range

Fifteen standards for the 1-2PP derivative were analyzed with the recommended analytical parameters described in OSHA Method 5002. These standards ranged from 0.1 to 2.0 times the analyte concentration in solvent that would be obtained from sampling the underivatized analyte for the recommended time at the target concentration. An ordinary least-squares linear regression curve was created by plotting the analyte mass per sample versus the corresponding area count of the analyte derivative peak. The resulting data provided the standard error of estimate (Calibration $S_{y/x}$) value across the calibration range, which provides an indication of the imprecision attributable to the instrumental analysis of the target analyte. Results from these analyses are listed in Table E-3, and plotted in Figure E-3.

Table E-3. Analytical precision data for the 1,6-hexamethylene diisocyanate homopolymer 1-2PP derivative (concentration as the underivatized analyte).

× target	0.1×	0.5×	1.0×	1.5×	2.0×
concn (µg/sample)	0.766	3.83	7.64	11.4	15.2
area counts x 10^4 (µV·s)	166.1	788.4	1608	2402	3160
	163.8	788.3	1635	2434	3158
	164.9	794.4	1607	2405	3128

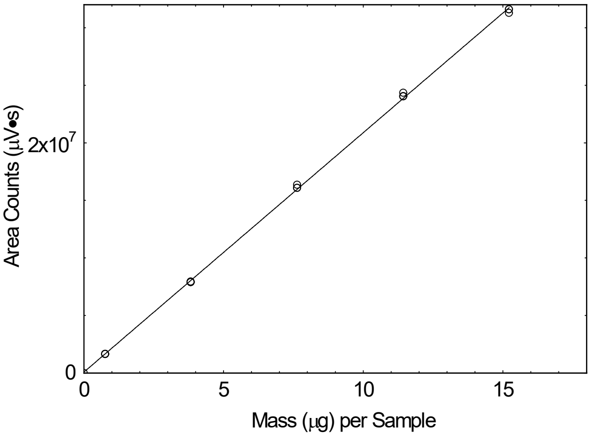

Figure E-3. Plot of data used to determine the precision of the analytical method for the 1,6-hexamethylene diisocyanate homopolymer 1-2PP derivative (as the underivatized analyte, $y = 2{,}083{,}015x + 89{,}406$, Calibration $S_{y/x}$ = 251,981).

4 Sampler Storage Stability

Storage stability test samples were prepared by spiking the 1,6-hexamethylene diisocyanate homopolymer 1-2PP derivative onto coated filters. The mass of the 1,6-hexamethylene diisocyanate homopolymer 1-2PP derivative spiked was stoichiometrically equivalent to the mass of the underivatized analyte that would be sampled at the target concentration (calculated to be 0.601 mg/m^3) in air for 15 min at a flow rate of 1.0 L/min. Humid air (81.0% relative humidity at 22.0 °C) was then drawn through each filter following the recommended sampling parameters published in OSHA Method 5002. Eighteen such storage samples were prepared and three of these were analyzed on the same day that samples were created. The remaining fifteen samples were stored in a closed drawer at ambient temperature (about 22.0 °C). Three samples were selected and analyzed from those remaining at 3-4 day intervals. The results of these analyses (uncorrected for extraction efficiency) are provided in Table E-4 and in Figure E-4.

The recovery of the 1,6-hexamethylene diisocyanate homopolymer 1-2PP derivative calculated from the regression line generated for the 17-day ambient storage test was 100.8%.

Table E-4. Sampler storage stability data for the 1,6-hexamethylene diisocyanate homopolymer 1-2PP derivative.

time (days)	ambient storage recovery (%)		
0	99.4	100.4	99.1
3	99.7	100.1	99.2
7	100.8	100.7	100.9
10	99.2	102.0	101.3
14	101.7	101.8	101.8
17	99.9	99.2	99.0

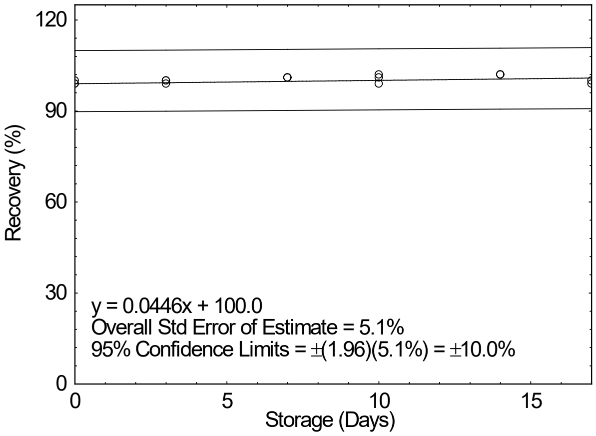

Figure E-4. Plot of ambient storage stability data for the 1,6-hexamethylene diisocyanate homopolymer 1-2PP derivative.

5 Precision of the Overall Procedure

The overall standard error of estimate obtained from the ambient storage test analyses described in Section 4 and sampling pump variability were used to determine the precision of the overall procedure, where all aspects of sampling and analysis (sampling, filter handling and solvent extraction, and instrumental analysis) are considered. This value was obtained by taking the square root of the squared ambient storage stability standard error of estimate (Storage $S^2_{y/x}$) added to the squared sampling pump variability value (V^2_{SP}). The resulting precision of the overall procedure at the 95% confidence level for the ambient 17-day storage test (at the target concentration) for the 1,6-hexamethylene diisocyanate homopolymer 1-2PP derivative was determined to be ±10.0% based on the observed ambient Storage $S_{y/x}$ value of 5.1% and V_{SP} value of 5.0%.

6 Recovery and Stability of Prepared Samples

Quantitative extraction is affected by the extraction solvent, the sampling medium, and the technique used to extract samples. The data presented demonstrate validity for the extraction solvent, sampling medium and extraction technique described in OSHA Method 5002. If other combinations of these are to be used, testing must be completed to satisfy the requirements found in current OSHA sampling and analysis method validation guidelines. Acceptable testing results must be documented.

A value for extraction efficiency (E_E) was determined by spiking the 1,6-hexamethylene diisocyanate homopolymer 1-2PP derivative onto four coated filters across a range of analyte derivative mass values that would be obtained from sampling the underivatized analyte at 0.1 to 2 times the target concentration value for 15 min. Four filters were also spiked in this fashion at the target concentration after drawing humid air (80.0% relative humidity at 21.0 °C) through these filters at 1.0 L/min for 15 min. All of the samples described above were analyzed the following day after being kept overnight at ambient temperature. The E_E value at the RQL was 100.5%, while that of the working range samples (excluding samples through which humid air had been drawn) was 100.5%. The data are shown in Table E-5. Pre-loading filters with moisture ("wet" designation in the table) did not have an unacceptable effect on E_E.

Table E-5. Extraction efficiency data for the 1,6-hexamethylene diisocyanate homopolymer 1-2PP derivative (μg per sample as the underivatized analyte).

level		sample number				
× target Concn	μg per sample	1	2	3	4	mean
0.1	0.770	96.2	97.4	99.2	98.7	97.9
0.25	1.92	100.3	99.3	101.9	100.8	100.6
0.5	3.83	100.3	101.6	103.1	101.8	101.7
1.0	7.66	101.6	101.5	101.2	101.5	101.4
1.5	11.5	101.4	101.2	99.2	99.2	100.2
2.0	15.3	100.6	102.4	100.3	100.6	101.0
RQL	0.271	102.5	98.4	102.9	98.4	100.5
1.0 (wet)	7.66	97.6	97.8	97.6	98.1	97.8

The stability of sample extracts prepared according to OSHA Method 5002 was examined by retaining the sample solvent extracts for the target concentration samples described immediately above. Two of the four vials were immediately recapped with new septa following the initial analyses, and again following each re-analysis event. The other two vials retained the original punctured septa throughout. All four vials were re-analyzed at 24, 48, and 72 hours after the initial analyses, with all vials remaining in an autosampler tray kept at 8.0 °C. Freshly prepared standards were used for each re-analysis event, and each septum (whether new or previously used) was punctured one time for each injection. The resulting data are shown in Table E-6.

Table E-6. Extracted sample stability data for the 1,6-hexamethylene diisocyanate homopolymer 1-2PP derivative.

	punctured septa replaced recovery (%)		punctured septa retained recovery (%)	
time (days)	1	2	1	2
0	105.0	104.9	104.7	104.9
1	102.8	103.2	105.5	103.1
2	103.3	104.2	102.6	100.6
3	103.8	104.9	106.2	104.5

7 Sampler Capacity

The sampling capacity of a coated filter was tested by performing a sample media analyte retention test. A filter to be spiked was mounted within a cassette in front of another coated filter, with a spacer separating the two filters. Six coated filters were liquid spiked with 1,6-hexamethylene-diisocyanate homopolymer 1-2PP derivative nominally at two times the target concentration (calculated to be 1.13 mg/m^3). Air was drawn through these samplers with a flow rate of 1.0 L/min for 20 min. The relative humidity and temperature were 80% and 21.0 °C. Breakthrough was not observed after sampling for 20 min (corresponding to 20 liters). Data from six coated samplers, as shown in Table E-7, were used to determine the recommended sampling volume of 15 liters for 1,6-hexamethylene-diisocyanate homopolymer as described in OSHA Method 5002. This volume corresponds to a 15 min sampling period, which is the maximum recommended sampling time regardless of breakthrough.

Table E-7. Retention data for the 1,6-hexamethylene diisocyanate homopolymer 1-2PP derivative.

sample no.	air volume (L)	recovery front (%)	recovery back (%)
1	20.0	96.6	0.0
2	20.0	98.5	0.0
3	20.0	98.7	0.0
4	20.0	99.0	0.0
5	20.0	97.7	0.0
6	20.0	99.0	0.0

8 Low Humidity

The effect of low humidity was tested by spiking six 1-2PP coated filters with the 1,6-hexamethylene diisocyanate homopolymer 1-2PP derivative in such a way that mass of the derivative spiked was stoichiometrically equivalent to the mass of underivatized analyte that would be sampled at twice the target concentration (calculated to be 1.13 mg/m^3) in air for 15 min at a flow rate of 1.0 L/min. Following this, dry air (15.0% relative humidity at 21.0 °C) was drawn through each filter in a cassette at 1.0 L/min for 20 min. After immediate analysis, results for the 1,6-hexamethylene diisocyanate homopolymer 1-2PP derivative as a percentage of expected recovery were 95.2%, 95.0%, 95.7%, 93.8%, 94.9%, and 95.1%.

9 Chemical Interference

The effect of potential chemical sampling interference was tested by spiking three 1-2PP coated filters with the 1,6-hexamethylene diisocyanate homopolymer 1-2PP derivative in such a way that mass of the derivative spiked was stoichiometrically equivalent to the mass of underivatized analyte that would be sampled at the target concentration (calculated to be 0.601 mg/m^3) in air for 15 min at a sampling rate of 1.0 L/min. Isophorone diisocyanate, methylene bis(4-cyclohexylisocyanate) and polymeric 4,4'-methylenediphenyl diisocyanate 1-2PP derivatives were also spiked at masses corresponding to sampling these as underivatized interferents under the same conditions at concentrations of 0.00500 ppm, 0.00562 ppm, and 0.495 mg/m^3 respectively. Following this, humid air (81.0% relative humidity at 22.0 °C) was drawn through each filter in a cassette at 1.0 L/min for 15 min. After immediate analysis, results for the 1,6-hexamethylene diisocyanate homopolymer 1-2PP derivative as a percentage of expected recovery were 99.4%, 100.4%, and 99.1%.

10 Analytical Method Reproducibility

Samples were prepared by spiking six 1-2PP coated filters with the 1,6-hexamethylene diisocyanate homopolymer 1,-2PP derivative in such a way that the mass of the derivative was approximately stoichiometrically equivalent to the mass of underivatized analyte that would be sampled at the target concentration in air for 15 min at a sampling rate of 1.0 L/min (calculated to be 0.633 mg/m^3). Following this, 15 L of humidified air (80.0% relative humidity at 21.0 °C) was drawn through each filter in a cassette. The resulting samples were submitted to the OSHA Salt Lake Technical Center for analysis using the procedures described in OSHA Method 5002 after ambient (22.0 °C) storage for 13 days. The analytical results corrected for E_E are provided in Table E-8. No sample result for the 1,6-hexamethylene diisocyanate homopolymer derivative fell outside the permissible bounds set by the precision of the overall procedure determined in Section 5 of this appendix.

Table E-8. Reproducibility data for the 1,6-hexamethylene diisocyanate homopolymer 1-2PP derivative (spiked and recovered μg/sample as the underivatized analyte).

spiked (μg/sample)	recovered (μg/sample)	recovery (%)	deviation (%)
9.49	9.32	98.2	-1.8
9.49	9.40	99.1	-0.9
9.49	9.19	96.8	-3.2
9.49	9.22	97.2	-2.8
9.49	9.27	97.7	-2.3
9.49	9.10	95.9	-4.1

11 Effect of Sampling a Low Concentration.

A study has not been undertaken to verify the effect of sampling a low concentration of 1,6-hexamethylene diisocyanate homopolymer aerosol.

12 Estimation of Uncertainty

While systematic biases such as analyte storage loss are examined, and limits are placed on these, an estimation of uncertainty that encompasses both potential random and systematic error was not completed. Instead, the overall standard error of estimate was calculated from the random error inherent to the points about the regression line produced by the ambient storage test described in Section 5, as prescribed by the OSHA validation guidelines in use at the time OSHA Method 5002 was originally validated. See Section 5 of this appendix for details.

13 Controlled Test Atmosphere Procedure

A controlled test atmosphere containing 1,6-hexamethylene diisocyanate homopolymer aerosol was not generated.

OSHA 5002, Appendix F
Isophorone Diisocyanate

Version:	1.0
OSHA PEL:	None
ACGIH TLV:	0.005 ppm (0.045 mg/m^3) 8-Hour TWA
Recommended sampling time and sampling rate:	15 min at 1.0 L/min (15 L)
Reliable quantitation limit:	0.63 ppb (5.7 μg/m^3)
Standard error of estimate:	5.2%
Status:	Fully validated. Method 5002 has been subjected to the established validation procedures of the Method Development Team for sampling and analysis of isophorone diisocyanate.

March 2003 (OSHA PV2034)
February 2021 (OSHA 5002)

David B. Armitage
Radhakrishnan Ukkiramapandian

1 Introduction

1.1 Previous Methods used by OSHA for Sampling and Analysis of Isophorone Diisocyanate

The specific analyte described in this appendix is isophorone diisocyanate CAS No. 4098-71-9. The methodologies described in this appendix for isophorone diisocyanate are based on OSHA Method PV2034.[1] That method requires the collection of samples using 1-(2-pyridyl)piperazine (1-2PP)-coated glass fiber filter, extraction using 90/10 (v/v) acetonitrile/dimethyl sulfoxide (ACN/DMSO), and analysis by liquid chromatography using a fluorescence detector.

1.2 Changes to the Previously-Used Method

This appendix represents an update of OSHA Method PV2034[1], which was partially validated at the time it was published based on the validation guidelines in effect at that time. Compared to the previous method used, this method includes new analytical parameters and extraction solvent volume. The data found in all subsequent sections of this appendix are new. The changes were made to allow the standardized collection and analysis of isophorone diisocyanate with other analytes found in Organic Vapor Sampling Group 3 described in OSHA Method 5002.

1.3 Validation Parameters

The procedures used to develop the method validation data are described in Validation Guidelines for Air Sampling Methods Utilizing Chromatographic Analysis.[2] Air concentrations listed in ppm are referenced to 25 °C and 760 Torr. The target concentration for method evaluation was the American Conference of Governmental Industrial Hygienists (ACGIH) 8-hour time-weighted average (TWA) Threshold Limit Value for isophorone diisocyanate.

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[1] Armitage, D. B., Isophorone Diisocyanate (OSHA Method PV2034), 1988. United States Department of Labor, Occupational Safety & Health Administration Web site. https://www.osha.gov/dts/sltc/methods/partial/pv2034/2034.html (accessed July 2020).

[2] Eide, M.; Simmons, M.; Hendricks, W. Validation Guidelines for Air Sampling Methods Utilizing Chromatographic Analysis, 2010. United States Department of Labor, Occupational Safety & Health Administration Web site. http://www.osha.gov/dts/sltc/methods/chromguide/chromguide.pdf (accessed July 2020).

2 Detection and Quantification

2.1 Detection Limit of the Analytical Procedure (DLAP)

The DLAP is the analyte mass introduced onto the chromatographic column that produces a response greater than 3× the standard error of estimate (DLAP $S_{y/x}$) divided by the slope of the line produced from analyses of ten analytical standards prepared with equally spaced increments of analyte derivative mass. The standards were prepared in such a way that the highest 1-2PP derivative standard concentration would produce a peak approximately 10 times the response of a reagent blank at or near the chromatographic retention time of the analyte derivative. The standards and a reagent blank were analyzed with the recommended analytical parameters described in OSHA Method 5002. The resulting data provided the DLAP $S_{y/x}$ and slope values for DLAP determination. Results obtained for these analyses are listed in Table F-1 and plotted in Figure F-1.

Table F-1. DLAP data for the isophorone diisocyanate 1-2PP derivative (concentration and mass on column as the underivatized analyte).

concentration (ng/mL)	mass on column (pg)	area counts (µV·s)
0.00	0.00	0.00
6.43	19.3	131,600
12.9	38.7	225,300
19.3	57.9	461,800
25.7	77.1	538,900
32.1	96.3	637,600
38.6	116	804,200
45.0	135	881,300
51.4	154	1091,000
57.8	173	1181,000
64.3	193	1278,000

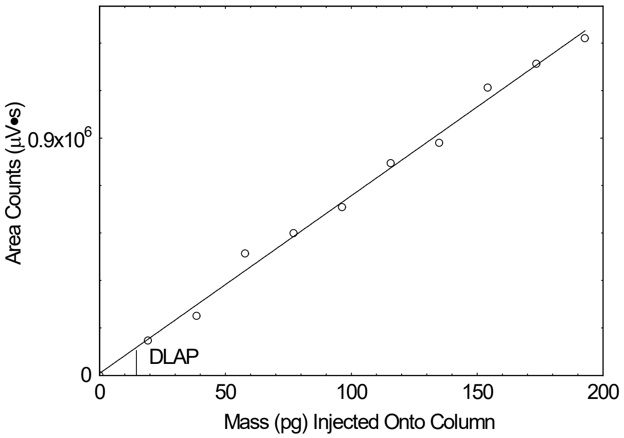

Figure F-1. Plot of data used to determine the DLAP of the isophorone diisocyanate 1-2PP derivative (as the underivatized analyte, $y = 6744x + 7327$, DLAP $S_{y/x}$ = 35,146, DLAP = 15.6 pg).

2.2 Detection Limit of the Overall Procedure (DLOP) and Reliable Quantitation Limit (RQL)

The DLOP is the analyte mass introduced onto the chromatographic column that produces a response greater than 3× the standard error of estimate (DLOP $S_{y/x}$) divided by the slope of the line produced from analyses of ten samples prepared from coated filters spiked with equally spaced increments of analyte derivative mass. The coated filters were spiked in such a way that the highest 1-2PP derivative mass loading produced a peak approximately 10 times greater than that of a sample blank at or near the chromatographic retention time of the analyte derivative. The RQL is expressed as an air concentration that will provide sufficient analyte mass per sample that produces a response greater than 10× DLOP $S_{y/x}$ divided by the slope of the line described above. The spiked samplers and a sample blank were analyzed with the recommended analytical parameters described in OSHA Method 5002. The resulting data provided the DLOP $S_{y/x}$ and slope values for DLOP and RQL determinations. Results obtained from these analyses are listed in Table F-2, and plotted in Figure F-2.

Table F-2. DLOP and RQL data for the isophorone diisocyanate 1-2PP derivative (mass per sample as the underivatized analyte).

mass per sample (ng/sample)	area counts (µV·s)
0.00	0.00
32.1	302,400
64.3	483,700
96.4	610,900
129	918,700
161	1,100,000
193	1,248,000
225	1,392,000
257	1,589,000
289	1,795,000
321	1,936,000

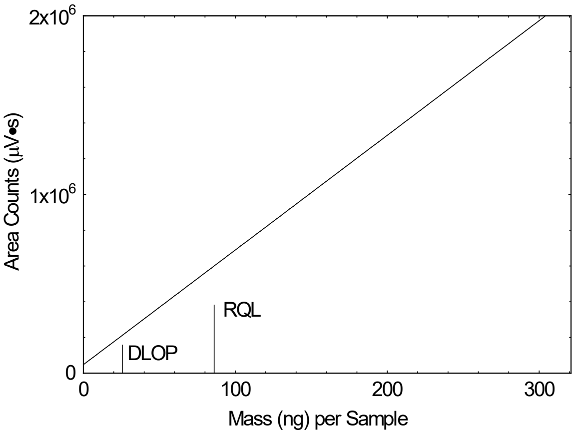

Figure F-2. Plot of data used to determine the DLOP and RQL for the isophorone diisocyanate 1-2PP derivative (as the underivatized analyte, $y = 5906x + 84{,}976$, DLOP $S_{y/x}$ = 50,267, DLOP = 25.5 ng/sample, RQL = 85.1 ng/sample or 0.624 ppb).

3 Analytical Precision Across the Calibration Range

Fifteen standards for the 1-2PP derivative were analyzed with the recommended analytical parameters described in OSHA Method 5002. These standards ranged from 0.1 to 2.0 times the analyte concentration in solvent that would be obtained from sampling the underivatized analyte for the recommended time at the target concentration. An ordinary least-squares linear regression curve was created by plotting the analyte mass per sample versus the corresponding area count of the analyte derivative peak. The resulting data provided the standard error of estimate (Calibration $S_{y/x}$) value across the calibration range, which provides an indication of the imprecision attributable to the instrumental analysis of the target analyte. Results from these analyses are listed in Table F-3, and plotted in Figure F-3.

Table F-3. Analytical precision data for the isophorone diisocyanate 1-2PP derivative (concentration as the underivatized analyte).

× target	0.1×	0.5×	1.0×	1.5×	2.0×
concn (µg/sample)	0.0640	0.321	0.640	0.959	1.28
area counts x 10^4 (µV·s)	44.72	214.8	428.7	650.0	865.3
	42.50	214.9	432.3	650.0	863.7
	43.05	214.4	427.8	654.6	878.8

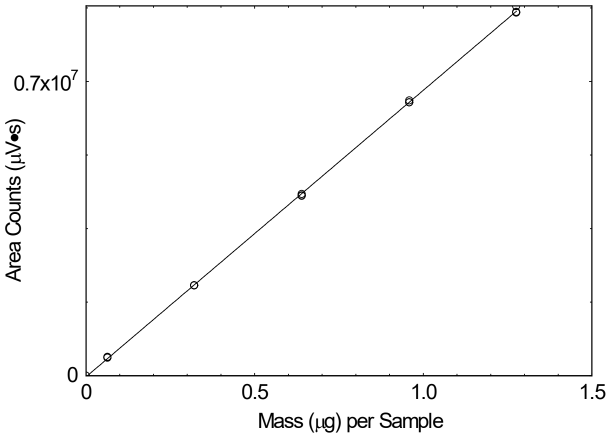

Figure F-3. Plot of data used to determine the precision of the analytical method for the isophorone diisocyanate 1-2PP derivative (as the underivatized analyte, $y = 6{,}804{,}512x - 24{,}939$, Calibration $S_{y/x}$ = 42,078).

4 Sampler Storage Stability

Storage stability test samples were prepared by spiking the isophorone diisocyanate 1-2PP derivative onto coated filters. The mass of the isophorone diisocyanate 1-2PP derivative spiked was stoichiometrically equivalent to the mass of the underivatized analyte that would be sampled at the target concentration (calculated to be 0.00471 ppm) in air for 15 min at a flow rate of 1.0 L/min. Humid air (81.0% relative humidity at 22.0 °C) was then drawn through each filter following the recommended sampling parameters published in OSHA Method 5002. Eighteen such storage samples were prepared and three of these were analyzed on the same day that samples were created. The remaining fifteen samples were stored in a closed drawer at ambient temperature (about 22.0 °C). Three samples were selected and analyzed from those remaining at 3-4 day intervals. The results of these analyses (uncorrected for extraction efficiency) are provided in Table F-4 and in Figure F-4.

The recovery of the isophorone diisocyanate 1-2PP derivative calculated from the regression line generated for the 17-day ambient storage test was 102.5%.

Table F-4. Sampler storage stability data for the isophorone diisocyanate 1-2PP derivative.

time (days)	ambient storage recovery (%)		
0	98.7	99.2	97.7
3	99.7	100.5	100.0
7	101.2	102.3	102.5
10	100.5	103.6	102.8
14	103.0	102.6	103.5
17	100.9	100.0	100.7

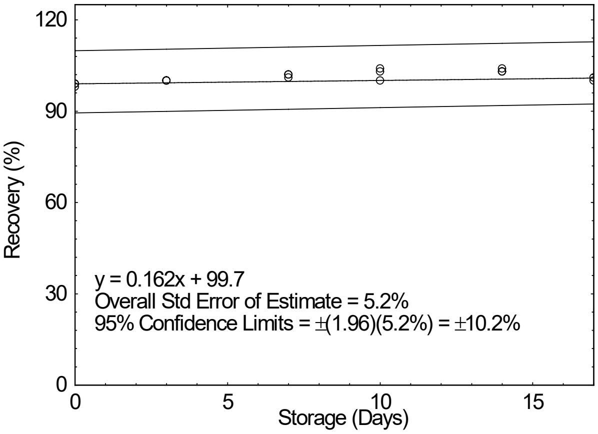

Figure F-4. Plot of ambient storage stability data for the isophorone diisocyanate 1-2PP derivative.

5 Precision of the Overall Procedure

The overall standard error of estimate obtained from the ambient storage test analyses described in Section 4 and sampling pump variability were used to determine the precision of the overall procedure, where all aspects of sampling and analysis (sampling, filter handling and solvent extraction, and instrumental analysis) are considered. This value was obtained by taking the square root of the squared ambient storage stability standard error of estimate (Storage $S_{y/x}^2$) added to the squared sampling pump variability value (V_{SP}^2). The resulting precision of the overall procedure at the 95% confidence level for the ambient 17-day storage test (at the target concentration) for the isophorone diisocyanate 1-2PP derivative was determined to be ±10.2% based on the observed ambient Storage $S_{y/x}$ value of 5.2% and V_{SP} value of 5.0%.

6 Recovery and Stability of Prepared Samples

Quantitative extraction is affected by the extraction solvent, the sampling medium, and the technique used to extract samples. The data presented demonstrate validity for the extraction solvent, sampling medium and extraction technique described in OSHA Method 5002. If other combinations of these are to be used, testing must be completed to satisfy the requirements found in current OSHA sampling and analysis method validation guidelines. Acceptable testing results must be documented.

A value for extraction efficiency (E_E) was determined by spiking the isophorone diisocyanate 1-2PP derivative onto four 1-2PP coated filters across a range of analyte derivative mass values that would be obtained from sampling the underivatized analyte at 0.1 to 2 times the target concentration value for 15 min. Four filters were also spiked in this fashion at the target concentration after drawing humid air (80.0% relative humidity at 21.0 °C) through these filters at 1.0 L/min for 15 min. All of the samples described above were analyzed the following day after being kept overnight at ambient temperature. The E_E value at the RQL was 105.3%, while that of the working range samples (excluding samples through which humid air had been drawn) was 101.6%. The data are shown in Table F-5. Pre-loading filters with moisture ("wet" designation in the table) did not have an unacceptable effect on E_E.

Table F-5. Extraction efficiency data for the isophorone diisocyanate 1-2PP derivative (µg per sample as the underivatized analyte).

level		sample number				
× target concn	µg per sample	1	2	3	4	mean
0.1	0.0600	105.7	104.0	104.0	105.7	104.8
0.25	0.161	104.4	104.4	104.4	104.4	104.4
0.5	0.321	101.1	101.1	101.1	101.1	101.1
1.0	0.642	99.5	99.5	101.1	101.1	100.3
1.5	0.960	99.6	99.6	98.6	99.6	99.4
2.0	1.28	99.7	99.7	100.5	99.0	99.7
RQL	0.0600	105.7	104.0	104.0	107.4	105.3
1.0 (wet)	0.642	101.1	101.1	102.6	97.9	100.7

The stability of sample extracts prepared according to OSHA Method 5002 was examined by retaining the sample solvent extracts for the target concentration samples described immediately above. Two of the four vials were immediately recapped with new septa following the initial analyses, and again following each re-analysis event. The other two vials retained the original punctured septa throughout. All four vials were re-analyzed at 24, 48, and 72 hours after the initial analyses, with all vials remaining in an autosampler tray kept at 8.0 °C. Freshly prepared standards were used for each re-analysis event, and each septum (whether new or previously used) was punctured one time for each injection. The resulting data are shown in Table F-6.

Table F-6. Extracted sample stability data for the isophorone diisocyanate 1-2PP derivative.

	punctured septa replaced recovery (%)		punctured septa retained recovery (%)	
time (days)	1	2	1	2
0	101.8	101.3	102.7	101.3
1	103.1	101.5	102.4	100.8
2	101.8	101.3	101.7	100.8
3	101.5	101.2	102.8	101.0

7 Sampler Capacity

The sampling capacity of a coated filter was tested by performing a sample media analyte retention test. A filter to be spiked was mounted within a cassette in front of another coated filter, with a spacer separating the two filters. Six coated filters were liquid spiked with Isophorone diisocyanate 1-2PP derivative nominally at two times the target concentration (calculated to be 0.00880 ppm). Air was drawn through these samplers with a flow rate of 1.0 L/min for 20 min. The relative humidity and temperature were 80% and 21.0 °C. Breakthrough was not observed after sampling for 20 min (corresponding to 20 liters). Data from six coated samplers, as shown in Table F-7, were used to determine the recommended sampling volume of 15 liters for isophorone diisocyanate as described in OSHA Method 5002. This volume corresponds to a 15 min sampling period, which is the maximum recommended sampling time regardless of breakthrough.

Table F-7. Retention data for the isophorone diisocyanate 1-2PP derivative.

sample no.	air volume (L)	recovery front (%)	recovery back (%)
1	20.0	95.7	0.0
2	20.0	97.7	0.0
3	20.0	97.9	0.0
4	20.0	97.9	0.0
5	20.0	96.8	0.0
6	20.0	97.8	0.0

8 Low Humidity

The effect of low humidity was tested by spiking six 1-2PP coated filters with the isophorone diisocyanate 1-2PP derivative in such a way that the mass of the derivative spiked was stoichiometrically equivalent to the mass of underivatized analyte that would be sampled at twice the target concentration (calculated to be 0.00880 ppm) in air for 15 min at a flow rate of 1.0 L/min. Following this, dry air (15.0% relative humidity at 21.0 °C) was drawn through each filter in a cassette at 1.0 L/min for 20 min. After immediate analysis, results for the isophorone diisocyanate 1-2PP derivative as a percentage of expected recovery were 105.6%, 108.0%, 108.5%, 106.5%, 107.9%, and 107.9%.

9 Chemical Interference

The effect of potential chemical sampling interference was tested by spiking three 1-2PP coated filters with the isophorone diisocyanate 1-2PP derivative in such a way that the mass of the derivative spiked was stoichiometrically equivalent to the mass of underivatized analyte that would be sampled at the target concentration (calculated to be 0.00500 ppm) in air for 15 min at a sampling rate of 1.0 L/min. 1,6-Hexamethylene diisocyanate homopolymer, methylene bis(4-cyclohexylisocyanate), and polymeric 4,4'-methylenediphenyl diisocyanate derivatives were also spiked at masses corresponding to sampling these as underivatized interferents under the same conditions at concentrations of 0.601 mg/m^3, 0.00562 ppm, and 0.495 mg/m^3 respectively. Following this, humid air (81.0% relative humidity at 22.0 °C) was drawn through each filter in a cassette at 1.0 L/min for 15 min. After immediate analysis, results for the isophorone diisocyanate 1-2PP derivative as a percentage of expected recovery were 98.7%, 99.2%, and 97.7%.

10 Analytical Method Reproducibility

Samples were prepared by spiking six 1-2PP coated filters with the isophorone diisocyanate 1-2PP derivative in such a way that the mass of the derivative was approximately stoichiometrically equivalent to the mass of underivatized analyte that would be sampled at the target concentration in air for 15 min at a sampling rate of 1.0 L/min (calculated to be 0.00566 ppm). Following this, 15 L of humid air (80.0% relative humidity at 21.0 °C) was drawn through each filter in a cassette. The resulting samples were submitted to the OSHA Salt Lake Technical Center for analysis using the procedures described in OSHA Method 5002 after ambient (22.0 °C) storage for 13 days. The analytical results corrected for E_E are provided in Table F-8. No sample result for isophorone diisocyanate fell outside the permissible bounds set by the precision of the overall procedure determined in Section 5 of this appendix.

Table F-8. Reproducibility data for the isophorone diisocyanate 1-2PP derivative (spiked and recovered μg/sample as the underivatized analyte).

spiked (μg/sample)	recovered (μg/sample)	recovery (%)	deviation (%)
0.771	0.819	106.2	+6.2
0.771	0.810	105.1	+5.1
0.771	0.791	102.6	+2.6
0.771	0.803	104.2	+4.2
0.771	0.789	102.3	+2.3
0.771	0.781	101.3	+1.3

11 Effect of Sampling a Low Concentration

A study has not been undertaken to verify the effect of sampling a low concentration of isophorone diisocyanate vapor.

12 Estimation of Uncertainty

While systematic biases such as analyte storage loss are examined, and limits are placed on these, an estimation of uncertainty that encompasses both potential random and systematic error was not completed. Instead, the overall standard error of estimate was calculated from the random error inherent to the points about the regression line produced by the ambient storage test described in Section 5, as prescribed by the OSHA validation guidelines in use at the time OSHA method 5002 was originally validated. See Section 5 of this appendix for details.

13 Controlled Test Atmosphere Procedure

A controlled test atmosphere containing isophorone diisocyanate vapor was not generated.

OSHA 5002, Appendix G
Methylene Bis(4-Cyclohexylisocyanate)

Version:	1.0
OSHA PEL:	None
ACGIH TLV:	0.005 ppm (0.054 mg/m^3) 8-Hour TWA
Recommended sampling time and sampling rate:	15 min at 1.0 L/min (15 L)
Reliable quantitation limit:	0.68 ppb (7.3 μg/m^3)
Standard error of estimate:	5.1%
Status:	Fully validated. Method 5002 has been subjected to the established validation procedures of the Method Development Team for sampling and analysis of methylene bis(4-cyclohexylisocyanate).

March 1988 (OSHA PV2092)
February 2021 (OSHA 5002)

David B. Armitage
Radhakrishnan Ukkiramapandian

1 Introduction

1.1 Previous Methods used by OSHA for Sampling and Analysis of Methylene Bis(4-Cyclohexylisocyanate)

The specific analyte described in this appendix is methylene bis(4-cyclohexylisocyanate) CAS No. 5124-30-1. The methodologies described in this appendix for methylene bis(4-cyclohexylisocyanate) are based on OSHA Method PV2092.[1] That method requires the collection of samples using a 1-(2-pyridyl)piperazine (1-2PP)-coated glass fiber filter, extraction using 90/10 (v/v) acetonitrile/dimethyl sulfoxide (ACN/DMSO), and analysis by liquid chromatography using a fluorescence detector.

1.2 Changes to the Previously-Used Method

This appendix represents an update of OSHA Method PV2092[1], which was partially validated at the time it was published based on the validation guidelines in effect at that time. Compared to the previous method used, this method includes new analytical parameters and extraction solvent volume. The data found in all subsequent sections of this appendix are new. The changes were made to allow the standardized collection and analysis of methylene bis(4-cyclohexylisocyanate) with other analytes found in Organic Vapor Sampling Group 3 described in OSHA Method 5002.

1.3 Validation Parameters

The procedures used to develop the method validation data are described in Validation Guidelines for Air Sampling Methods Utilizing Chromatographic Analysis.[2] Air concentrations listed in ppm are referenced to 25 °C and 760 Torr. The target concentration for method evaluation was the American Conference of Governmental Industrial Hygienists (ACGIH) 8-hour time-weighted average (TWA) Threshold Limit Value for methylene bis(4-cyclohexylisocyanate).

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[1] Armitage, D. B., Methylene bis (4-cyclohexylisocyanate) (OSHA Method PV2092), 1988. United States Department of Labor, Occupational Safety & Health Administration Web site. https://www.osha.gov/dts/sltc/methods/partial/t-pv2092-01-8804-ch/t-pv2092-01-8804-ch.html (accessed July 2020).

[2] Eide, M.; Simmons, M.; Hendricks, W. Validation Guidelines for Air Sampling Methods Utilizing Chromatographic Analysis, 2010. United States Department of Labor, Occupational Safety & Health Administration Web site. http://www.osha.gov/dts/sltc/methods/chromguide/chromguide.pdf (accessed July 2020).

2 Detection and Quantification

2.1 Detection Limit of the Analytical Procedure (DLAP)

The DLAP is the analyte mass introduced onto the chromatographic column that produces a response greater than 3× the standard error of estimate (DLAP $S_{y/x}$) divided by the slope of the line produced from analyses of ten analytical standards prepared with equally spaced increments of analyte derivative mass. The standards were prepared in such a way that the highest 1-2PP derivative standard concentration would produce a peak approximately 10 times the response of a reagent blank at or near the chromatographic retention time of the analyte derivative. The standards and a reagent blank were analyzed with the recommended analytical parameters described in OSHA Method 5002. The resulting data provided the DLAP $S_{y/x}$ and slope values for DLAP determination. Results obtained for these analyses are listed in Table G-1 and plotted in Figure G-1.

Table G-1. DLAP data for the methylene bis(4-cyclohexylisocyanate) 1-2PP derivative (concentration and mass on column as the underivatized analyte).

concentration (ng/mL)	mass on column (pg)	area counts (μV·s)
0.00	0.00	0.00
3.72	11.2	96,300
7.45	22.4	258,600
11.2	33.6	317,700
14.9	44.7	362,400
18.6	55.8	390,800
22.3	66.9	479,100
26.1	78.3	537,300
29.8	89.4	604,600
33.5	101	627,800
37.2	112	722,100

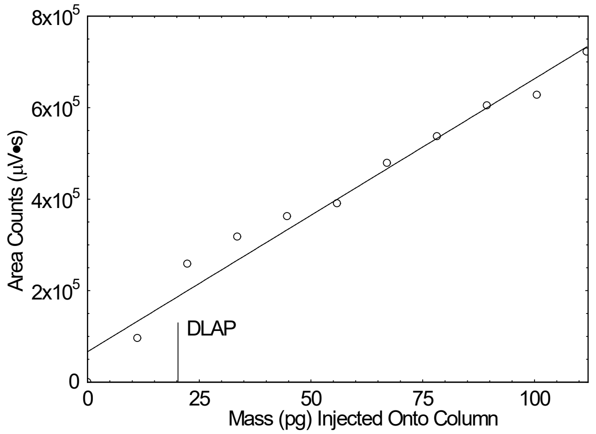

Figure G-1. Plot of data used to determine the DLAP for the methylene bis(4-cyclohexylisocyanate) 1-2PP derivative (as the underivatized analyte, $y = 5950x + 66{,}886$, DLAP $S_{y/x}$ = 40,532, DLAP = 20.4 pg).

2.2 Detection Limit of the Overall Procedure (DLOP) and Reliable Quantitation Limit (RQL)

The DLOP is the analyte mass introduced onto the chromatographic column that produces a response greater than 3× the standard error of estimate (DLOP $S_{y/x}$) divided by the slope of the line produced from analyses of ten samples prepared from coated filters spiked with equally spaced increments of analyte derivative mass. The coated filters were spiked in such a way that the highest 1-2PP derivative mass loading produced a peak approximately 10 times greater than that of a sample blank at or near the chromatographic retention time of the analyte derivative. The RQL is expressed as an air concentration that will provide sufficient analyte mass per sample that produces a response greater than 10× DLOP $S_{y/x}$divided by the slope of the line described above. The spiked samplers and a sample blank were analyzed with the recommended analytical parameters described in OSHA Method 5002.The resulting data provided the DLOP $S_{y/x}$ and slope values for DLOP and RQL determinations. Results obtained from these analyses are listed in Table G-2, and plotted in Figure G-2.

Table G-2. DLOP and RQL data for the methylene bis(4-cyclohexylisocyanate) 1-2PP derivative (mass per sample as the underivatized analyte).

mass per sample (ng/sample)	area counts (μV·s)
0.00	0.00
37.2	653,500
74.5	1,357,000
112	2,060,000
149	2,771,000
186	3,727,000
223	4,471,000
261	5,949,000
298	6,777,000
335	7,507,000
372	8,256,000

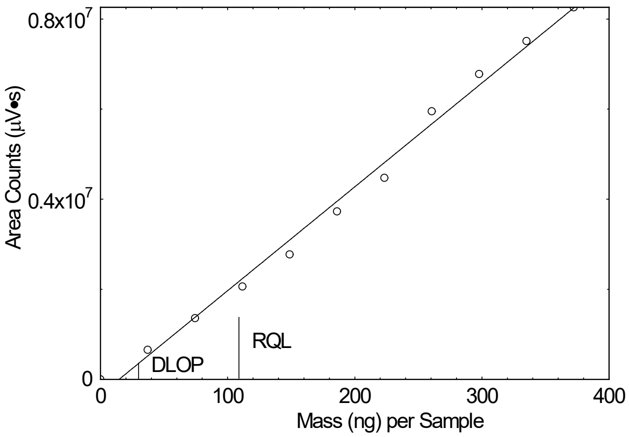

Figure G-2. Plot of data used to determine the DLOP and RQL for the methylene bis(4-cyclohexylisocyanate) 1-2PP derivative (as the underivatized analyte), $y = 23{,}069x - 337{,}258$, DLOP $S_{y/x}$ = 254,012, DLOP = 33.0 ng/sample, RQL = 110 ng/sample or 0.683 ppb).

3 Analytical Precision Across the Calibration Range

Fifteen standards for the 1-2PP derivative were analyzed with the recommended analytical parameters described in OSHA Method 5002. These standards ranged from 0.1 to 2.0 times the analyte concentration in solvent that would be obtained from sampling the underivatized analyte for the recommended time at the target concentration. An ordinary least-squares linear regression curve was created by plotting the analyte mass per sample versus the corresponding peak area count of the analyte derivative peak. The resulting data provided the standard error of estimate (Calibration $S_{y/x}$) value across the calibration range, which provides an indication of the imprecision attributable to the instrumental analysis of the target analyte. Results from these analyses are listed in Table G-3, and plotted in Figure G-3.

Table G-3. Analytical precision data for the methylene bis(4-cyclohexylisocyanate) 1-2PP derivative (concentration as the underivatized analyte).

× target	0.1×	0.5×	1.0×	1.5×	2.0×
concn (μg/sample)	0.0900	0.452	0.902	1.35	1.80
area counts x 10^4 (μV·s)	44.90	220.8	438.3	656.8	877.7
	43.23	217.4	439.3	658.7	878.7
	44.39	219.0	435.8	664.6	889.1

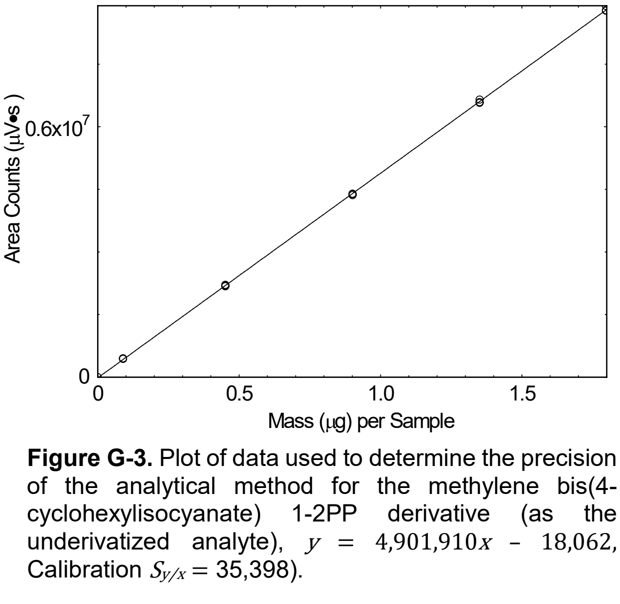

Figure G-3. Plot of data used to determine the precision of the analytical method for the methylene bis(4-cyclohexylisocyanate) 1-2PP derivative (as the underivatized analyte), $y = 4{,}901{,}910x - 18{,}062$, Calibration $S_{y/x}$ = 35,398).

4 Sampler Storage Stability

Storage stability test samples were prepared by spiking the methylene bis(4-cyclohexylisocyanate) 1-2PP derivative onto coated filters. The mass of the methylene bis(4-cyclohexylisocyanate) 1-2PP derivative spiked was stoichiometrically equivalent to the mass of the underivatized analyte that would be sampled at the target concentration (calculated to be 0.00563 ppm) in air for 15 min at a flow rate of 1.0 L/min. Humid air (81.0% relative humidity at 22.0 °C) was then drawn through each filter following the recommended sampling parameters published in OSHA Method 5002. Eighteen such storage samples were prepared and three of these were analyzed on the same day that samples were created. The remaining fifteen samples were stored in a closed drawer at ambient temperature (about 22.0 °C). Three samples were selected and analyzed from those remaining at 3-4 day intervals. The results of these analyses (uncorrected for extraction efficiency) are provided in Table G-4 and in Figure G-4.

The recovery of the methylene bis(4-cyclohexylisocyanate) 1-2PP derivative calculated from the regression line generated for the 17-day ambient storage test was 100.8%.

Table G-4. Sampler storage stability data for the methylene bis(4-cyclohexylisocyanate) 1-2PP derivative.

time (days)	ambient storage recovery (%)		
0	98.9	99.4	97.9
3	98.8	98.9	98.6
7	100.2	100.7	100.9
10	98.3	101.9	101.6
14	100.8	101.7	101.1
17	100.1	99.5	99.5

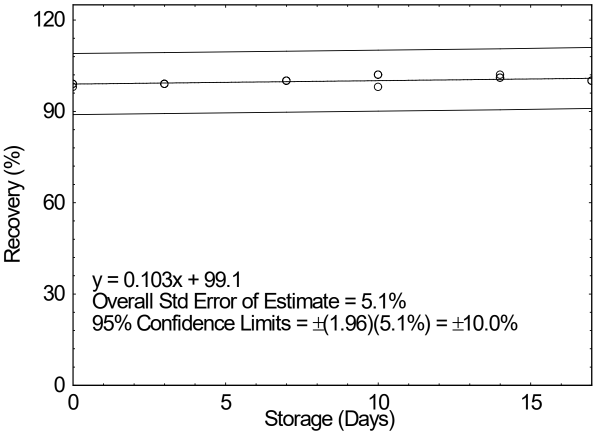

Figure G-4. Plot of ambient storage stability data for the methylene bis(4-cyclohexylisocyanate) 1-2PP derivative.

5 Precision of the Overall Procedure

The overall standard error of estimate obtained from the ambient storage test analyses described in Section 4 and sampling pump variability were used to determine the precision of the overall procedure, where all aspects of sampling and analysis (sampling, filter handling and solvent extraction, and instrumental analysis) are considered. This value was obtained by taking the square root of the squared ambient storage stability standard error of estimate (Storage $S_{y/x}^2$) added to the squared sampling pump variability value (V_{SP}^2). The resulting precision of the overall procedure at the 95% confidence level for the ambient 17-day storage test (at the target concentration) for the methylene bis(4-cyclohexylisocyanate) 1-2PP derivative was determined to be ±10.0% based on the observed ambient Storage $S_{y/x}$ value of 5.1% and V_{SP} value of 5.0%.

6 Recovery and Stability of Prepared Samples

Quantitative extraction is affected by the extraction solvent, the sampling medium, and the technique used to extract samples. The data presented demonstrate validity for the extraction solvent, sampling medium and extraction technique described in OSHA Method 5002. If other combinations of these are to be used, testing must be completed to satisfy the requirements found in current OSHA sampling and analysis method validation guidelines. Acceptable testing results must be documented.

A value for extraction efficiency (*E_E*) was determined by spiking the methylene bis(4-cyclohexylisocyanate) 1-2PP derivative onto four 1-2PP coated filters across a range of analyte derivative mass values that would be obtained from sampling the underivatized analyte at 0.1 to 2 times the target concentration value for 15 min. Four filters were also spiked in this fashion at the target concentration after drawing humid air (80.0% relative humidity at 21.0 °C) through these filters at 1.0 L/min for 15 min. All of the samples described above were analyzed the following day after being kept overnight at ambient temperature. The E_E value at the RQL was 99.1%, while that of the working range samples (excluding samples through which humid air had been drawn) was 99.8%. The data are shown in Table G-5. Pre-loading filters with moisture ("wet" designation in the table) did not have an unacceptable effect on E_E.

Table G-5. Extraction efficiency data for the methylene bis(4-cyclohexylisocyanate) 1-2PP derivative (µg per sample as the underivatized analyte).

level		sample number				
× target concn	µg per sample	1	2	3	4	mean
0.1	0.0910	101.8	98.6	97.5	101.8	99.9
0.25	0.226	104.4	100.0	100.0	100.0	101.1
0.5	0.453	99.3	99.3	99.3	99.3	99.3
1.0	0.905	98.9	98.9	100.0	100.0	99.5
1.5	1.36	99.5	99.5	99.5	99.5	99.5
2.0	1.81	100.0	99.5	100.5	98.9	99.7
RQL	0.0910	97.6	98.6	101.8	98.6	99.1
1.0 (wet)	0.905	100.0	100.0	101.1	96.7	99.5

The stability of sample extracts prepared according to OSHA Method 5002 was examined by retaining the sample solvent extracts for the target concentration samples described immediately above. Two of the four vials were immediately recapped with new septa following the initial analyses, and again following each re-analysis event. The other two vials retained the original punctured septa throughout. All four vials were re-analyzed at 24, 48, and 72 hours after the initial analyses, with all vials remaining in an autosampler tray kept at 8.0 °C. Freshly prepared standards were used for each re-analysis event, and each septum (whether new or previously used) was punctured once for each injection. The resulting data are shown in Table G-6.

Table G-6. Extracted sample stability data for the methylene bis(4-cyclohexylisocyanate) 1-2PP derivative.

	punctured septa replaced recovery (%)		punctured septa retained recovery (%)	
time (days)	1	2	1	2
0	100.9	101.2	100.7	101.0
1	101.7	101.2	100.8	100.5
2	100.6	100.8	100.0	100.5
3	100.7	100.5	101.1	100.5

7 Sampler Capacity

The sampling capacity of a coated filter was tested by performing a sample media analyte retention test. A filter to be spiked was mounted within a cassette in front of another coated filter, with a spacer separating the two filters. Six coated filters were liquid spiked with methylene bis(4-cyclohexylisocyanate) 1-2PP derivative nominally two times the target concentration (calculated to be 0.0105 ppm). Air was drawn through these samplers with a flow rate of 1.0 L/min for 20 min. The relative humidity and temperature were 80% and 21.0 °C. Breakthrough was not observed after sampling for 20 min (corresponding to 20 liters). Data from six coated samplers, as shown in Table G-7, were used to determine the recommended sampling volume of 15 liters for methylene bis(4-cyclohexylisocyanate) as described in OSHA

Method 5002. This volume corresponds to a 15 min sampling period, which is the maximum recommended sampling time regardless of breakthrough.

Table G-7. Retention data for the methylene bis(4-cyclohexylisocyanate) 1-2PP derivative.

sample no.	air volume (L)	recovery front (%)	recovery back (%)
1	20.0	95.4	0.0
2	20.0	96.7	0.0
3	20.0	96.7	0.0
4	20.0	97.2	0.0
5	20.0	96.8	0.0
6	20.0	98.3	0.0

8 Low Humidity

The effect of low humidity was tested by spiking six 1-2PP coated filters with the methylene bis(4-cyclohexylisocyanate) 1-2PP derivative in such a way that the mass of the derivative spiked was stoichiometrically equivalent to the mass of underivatized analyte that would be sampled at twice the target concentration (calculated to be 0.0105 ppm) in air for 15 min at a flow rate of 1.0 L/min. Following this, dry air (15.0% relative humidity at 21.0 ˚C) was drawn through each filter in a cassette at 1.0 L/min for 20 min. After immediate analysis, results as a percentage of expected recovery for the methylene bis(4-cyclohexylisocyanate) 1-2PP derivative were 98.4%, 97.8%, 99.1%, 97.4%, 98.4% and 97.8%.

9 Chemical Interference

The effect of potential chemical sampling interference was tested by spiking three 1-2PP coated filters with the methylene bis(4-cyclohexylisocyanate) 1-2PP derivative in such a way that the mass of the derivative spiked was stoichiometrically equivalent to the mass of underivatized analyte that would be sampled at the target concentration (calculated to be 0.00562 ppm) in air for 15 min at a sampling rate of 1.0 L/min. Isophorone diisocyanate, 1,6-hexamethylene diisocyanate homopolymer, and polymeric 4,4’-methylenediphenyl diisocyanate 1-2PP derivatives were also spiked at masses corresponding to sampling these as underivatized interferents under the same conditions at concentrations of 0.00500 ppm, 0.601 mg/m^3, and 0.495 mg/m^3 respectively. Following this, humid air (81.0% relative humidity at 22.0 °C) was drawn through each filter in a cassette at 1.0 L/min for 15 min. After immediate analysis, results for the methylene bis(4-cyclohexylisocyanate) derivative as a percentage of expected recovery were 98.9%, 99.4%, and 97.9%.

10 Analytical Method Reproducibility

Samples were prepared by spiking six 1-2PP coated filters with the methylene bis(4-cyclohexylisocyanate) 1-2PP derivative in such a way that the mass of the derivative was approximately stoichiometrically equivalent to the mass of underivatized analyte that would be sampled at the target concentration in air for 15 min at a sampling rate of 1.0 L/min (calculated to be 0.00556 ppm). Following this, 15 L of humidified air (80.0% relative humidity at 21.0 °C) was drawn through each filter in a cassette. The resulting samples were submitted to the OSHA Salt Lake Technical Center for analysis using the procedures described in OSHA Method 5002 after ambient (22.0 °C) storage for 13 days. The analytical results corrected for E_E are provided in Table G-8. No sample result for methylene bis(4-cyclohexylisocyanate) fell outside the permissible bounds set by the precision of the overall procedure determined in Section 5 of this appendix.

Table G-8. Reproducibility data for the methylene bis(4-cyclohexylisocyanate) 1-2PP derivative (spiked and recovered μg/sample as the underivatized analyte).

spiked (μg/sample)	recovered (μg/sample)	recovery (%)	deviation (%)
0.894	0.893	99.9	-0.1
0.894	0.886	99.1	-0.9
0.894	0.859	96.1	-3.9
0.894	0.874	97.8	-2.2
0.894	0.868	97.1	-2.9
0.894	0.855	95.6	-4.4

11 Effect of Sampling a Low Concentration

A study has not been undertaken to verify the effect of sampling a low concentration of methylene bis(4-cyclohexylisocyanate) vapor.

12 Estimation of Uncertainty

While systematic biases such as analyte storage loss are examined, and limits are placed on these, an estimation of uncertainty that encompasses both potential random and systematic error was not completed. Instead, the overall standard error of estimate was calculated from the random error inherent to the points about the regression line produced by the ambient storage test described in Section 5, as prescribed by the OSHA validation guidelines in use at the time OSHA Method 5002 was originally validated. See Section 5 of this appendix for details.

13 Controlled Test Atmosphere Procedure

A controlled test atmosphere containing methylene bis(4-cyclohexylisocyanate) vapor was not generated.

OSHA 5002, Appendix H
Polymeric 4,4'-Methylenediphenyl Diisocyanate

Version:	1.0
OSHA PEL:	None
ACGIH TLV:	None
Recommended sampling time and sampling rate:	15 min at 1.0 L/min (15 L)
Reliable quantitation limit:	0.022 mg/m^3
Standard error of estimate:	5.5%
Status:	Fully validated. Method 5002 has been subjected to the established validation procedures of the Method Development Team for sampling and analysis of polymeric 4,4'-methylenediphenyl diisocyanate.

February 2021 (OSHA 5002) Radhakrishnan Ukkiramapandian

1 Introduction

1.1 Previous Methods used by OSHA for Sampling and Analysis of Polymeric 4,4'-Methylenediphenyl Diisocyanate

The specific analyte described in this appendix is polymeric 4,4'-methylenediphenyl diisocyanate CAS No. 9016-87-9. The methodologies described in this appendix for polymeric 4,4'-methylenediphenyl diisocyanate are based on OSHA Method OSHA 47.[1] That method requires the collection of samples using a 1-(2-pyridyl)piperazine (1-2PP)-coated glass fiber filter, extraction using 90/10 (v/v) acetonitrile/dimethyl sulfoxide (ACN/DMSO), and analysis by liquid chromatography using a fluorescence detector.

1.2 Changes to the Previously-Used Method

This appendix represents an update of OSHA Method 47[1], which was fully validated at the time it was published based on the validation guidelines in effect at that time. Compared to the previous method used, this method includes new analytical parameters and extraction solvent volume. The data found in all subsequent sections of this appendix are new. The changes were made to allow the standardized collection and analysis of polymeric 4,4'-methylenediphenyl diisocyanate with other analytes found in Organic Vapor Sampling Group 3 described in OSHA Method 5002. While the target analyte has no appreciable vapor pressure, the reactivity of its isocyanate functional groups with 1-2PP, and the ability for Method 5002 liquid chromatography methods to analyze the resulting derivatives make this method suitable for analysis of polymeric 4,4'-methylenediphenyl diisocyanate aerosol components.

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[1] Burright, D. Methylene bisphenyl isocyanate (MDI) (OSHA Method 47), 1989. United States Department of Labor, Occupational Safety & Health Administration Web site. https://www.osha.gov/dts/sltc/methods/organic/org047/org047.html (accessed July 2020).

1.3 Validation Parameters

The procedures used to develop the method validation data are described in Validation Guidelines for Air Sampling Methods Utilizing Chromatographic Analysis.[2] Air concentrations listed in ppm are referenced to 25 °C and 760 Torr. The target concentration for method evaluation was 0.500 mg/m^3 for polymeric 4,4'-methylenediphenyl diisocyanate.

2 Detection and Quantification

2.1 Detection Limit of the Analytical Procedure (DLAP)

The DLAP is the analyte mass introduced onto the chromatographic column that produces a response greater than 3× the standard error of estimate (DLAP $S_{y/x}$) divided by the slope of the line produced from analyses of ten analytical standards prepared with equally spaced increments of analyte derivative mass. The standards were prepared in such a way that the highest 1-2PP derivative standard concentration would produce a peak approximately 10 times the response of a reagent blank at or near the chromatographic retention time of the analyte derivative. The standards and a reagent blank were analyzed with the recommended analytical parameters described in OSHA Method 5002. The resulting data provided the DLAP $S_{y/x}$ and slope values for DLAP determination. Results obtained for these analyses are listed in Table H-1 and plotted in Figure H-1.

Table H-1. DLAP data for the polymeric 4,4'-methylenediphenyl diisocyanate 1-2PP derivative (concentration and mass on column as the underivatized analyte).

concentration (ng/mL)	mass on column (pg)	area counts (µV·s)
0.00	0.00	922,800
15.6	46.8	1,146,000
31.2	93.6	1,467,000
46.7	140	1,747,000
62.7	188	2,000,000
78.0	234	2,268,000
93.7	281	2,419,000
109	327	2,773,000
125	375	3,075,000
140	420	3,306,000
156	468	3,750,000

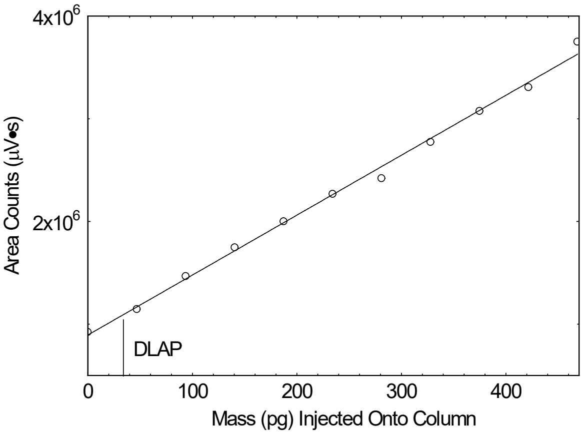

Figure H-1. Plot of data used to determine the DLAP for the polymeric 4,4'-methylenediphenyl diisocyanate 1-2PP derivative (as the underivatized analyte, $y = 5846x + 893{,}615$, DLAP $S_{y/x} = 61{,}990$, DLAP = 31.8 pg).

2.2 Detection Limit of the Overall Procedure (DLOP) and Reliable Quantitation Limit (RQL)

The DLOP is the analyte mass introduced onto the chromatographic column that produces a response greater than 3× the standard error of estimate (DLOP $S_{y/x}$) divided by the slope of the line produced from analyses of ten samples prepared from coated filters spiked with equally spaced increments of analyte derivative mass. Coated filters were spiked in such a way that the highest 1-2PP derivative mass loading produced a peak approximately 10 times greater than that of a sample blank at or near the chromatographic retention of time of the analyte derivative. The RQL is expressed as an air concentration that will provide sufficient analyte mass per sample that produces a response greater than 10× DLOP $S_{y/x}$divided by the slope of the line described above. The spiked samplers and a sample blank were analyzed with the recommended analytical parameters described in OSHA Method 5002.The resulting data provided the DLOP $S_{y/x}$ and slope values for DLOP and RQL determinations. Results obtained from these analyses are listed in

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[2] Eide, M.; Simmons, M.; Hendricks, W. Validation Guidelines for Air Sampling Methods Utilizing Chromatographic Analysis, 2010. United States Department of Labor, Occupational Safety & Health Administration Web site. http://www.osha.gov/dts/sltc/methods/chromguide/chromguide.pdf (accessed July 2020).

Table H-2, and plotted in Figure H-2.

Table H-2. DLOP and RQL data for the polymeric 4,4'-methylenediphenyl diisocyanate 1-2PP derivative (mass per sample as the underivatized analyte).

mass per sample (µg/sample)	area counts (µV·s)
0.00	235,100
0.312	1,984,000
0.624	3,743,000
0.936	5,430,000
1.25	7,170,000
1.56	8,771,000
1.87	10,790,000
2.18	12,500,000
2.50	13,900,000
2.81	15,610,000
3.12	16,970,000

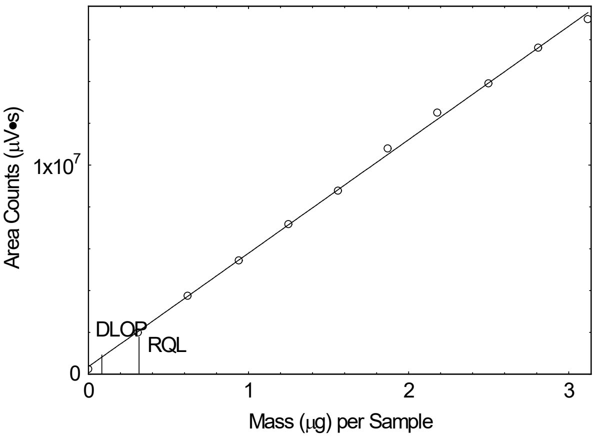

Figure H-2. Plot of data used to determine the DLOP and RQL for the polymeric 4,4'-methylenediphenyl diisocyanate 1-2PP derivative (as the underivatized analyte, $y = 5{,}430{,}072x + 355{,}655$, DLOP $S_{y/x}$ = 183,646, DLOP = 0.101 µg/sample, RQL = 0.338 µg/sample or 0.0225 mg/m^3).

3 Analytical Precision Across the Calibration Range

Fifteen standards for the 1-2PP derivative were analyzed with the recommended analytical parameters described in OSHA Method 5002. These standards ranged from 0.1 to 2.0 times the analyte concentration in solvent that would be obtained from sampling the underivatized analyte for the recommended time at the target concentration. An ordinary least-squares linear regression curve was created by plotting the analyte mass per sample versus the corresponding peak area count of the analyte derivative peak. The resulting data provided the standard error of estimate (Calibration $S_{y/x}$) value across the calibration range, which provides an indication of the imprecision attributable to the instrumental analysis of the target analyte. Results from theses analyses are listed in Table H-3, and plotted in Figure H-3.

Table H-3. Analytical precision data for the polymeric 4,4'-methylenediphenyl diisocyanate 1-2PP derivative (concentration as the underivatized analyte).

× target	0.1×	0.5×	1.0×	1.5×	2.0×
concn (µg/sample)	0.742	3.70	7.40	11.1	14.7
area counts x 10^4 (µV·s)	446.6	1987	3931	5876	7808
	420.8	1979	3960	5936	7858
	422.1	1988	3935	5948	7916

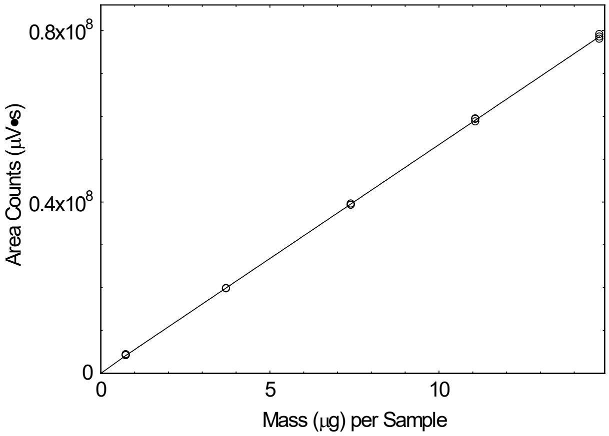

Figure H-3. Plot of data used to determine the precision of the analytical method for the polymeric 4,4'-methylenediphenyl diisocyanate 1-2PP derivative (as the underivatized analyte, $y = 5{,}323{,}247x + 198{,}799$, Calibration $S_{y/x}$ = 308,328).

4 Sampler Storage Stability

Storage stability test samples were prepared by spiking the polymeric 4,4’-methylenediphenyl diisocyanate 1-2PP derivative onto coated filters. The mass of the polymeric 4,4’-methylenediphenyl diisocyanate 1-2PP derivative spiked was stoichiometrically equivalent to the mass of the underivatized analyte that would be sampled at the target concentration (calculated to be 0.495 mg/m^3) in air for 15 min at a flow rate of 1.0 L/min. Humid air (81.0% relative humidity at 22.0 °C) was then drawn through each filter following the recommended sampling parameters published in OSHA Method 5002. Eighteen such storage samples were prepared and three of these were analyzed on the same day that samples were created. The remaining fifteen samples were stored in a closed drawer at ambient temperature (about 22.0 °C). Three samples were selected and analyzed from those remaining at 3-4 day intervals. The results of these analyses (uncorrected for extraction efficiency) are provided in Table H-4 and in Figure H-4.

The recovery of the polymeric 4,4’-methylenediphenyl diisocyanate 1-2PP derivative calculated from the regression line generated for the 17-day ambient storage test was 99.5%.

Table H-4. Sampler storage stability data for the polymeric 4,4’-methylenediphenyl diisocyanate 1-2PP derivative.

time (days)	ambient storage recovery (%)		
0	100.1	100.4	99.3
3	100.1	100.1	99.9
7	100.6	100.8	101.1
10	100.0	102.1	101.3
14	94.5	102.6	94.2
17	101.2	100.2	100.0

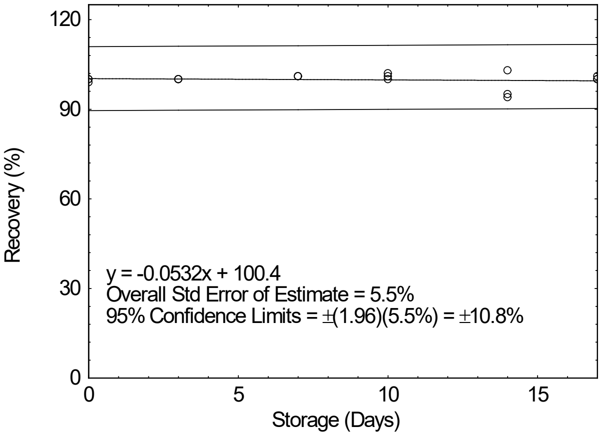

Figure H-4. Plot of ambient storage stability data for the polymeric 4,4’-methylenediphenyl diisocyanate 1-2PP derivative.

5 Precision of the Overall Procedure

The overall standard error of estimate obtained from the ambient storage test analyses described in Section 4 and sampling pump variability were used to determine the precision of the overall procedure, where all aspects of sampling and analysis (sampling, filter handling and solvent extraction, and instrumental analysis) are considered. This value was obtained by taking the square root of the squared ambient storage stability standard error of estimate (Storage $S^2_{y/x}$) added to the squared sampling pump variability value (V^2_{SP}). The resulting precision of the overall procedure at the 95% confidence level for the ambient 17-day storage test (at the target concentration) for the polymeric 4,4’-methylenediphenyl diisocyanate 1-2PP derivative was determined to be ±10.8% based on the observed ambient Storage $S_{y/x}$ value of 5.5% and V_{SP} value of 5.0%.

6 Recovery and Stability of Prepared Samples

Quantitative extraction is affected by the extraction solvent, the sampling medium, and the technique used to extract samples. The data presented demonstrate validity for the extraction solvent, sampling medium and extraction technique described in OSHA Method 5002. If other combinations of these are to be used, testing must be completed to satisfy the requirements found in current OSHA sampling and analysis method validation guidelines. Acceptable testing results must be documented.

A value for extraction efficiency (*E*) was determined by spiking the polymeric 4,4’-methylenediphenyl diisocyanate 1-2PP derivative onto four 1-2PP coated filters across a range of analyte derivative mass values that would be obtained from sampling the underivatized analyte at 0.1 to 2 times the target concentration value for 15 min. Four filters were also spiked in this fashion at the target concentration after drawing humid air (80.0% relative humidity at 21.0 °C) through these filters at 1.0 L/min for 15 min. All of the samples described above were analyzed the following day after being kept overnight at ambient temperature. The E_E value at the RQL was 94.4%, while that of the working range samples (excluding samples through which humid air had been drawn) was 101.4%. The data are shown in Table H-5. Pre-loading filters with moisture (“wet” designation in the table) did not have an unacceptable effect on E_E.

Table H-5. Extraction efficiency data for the polymeric 4,4’-methylenediphenyl diisocyanate 1-2PP derivative (µg per sample as the underivatized analyte).

level		sample number				
× target concn	µg per sample	1	2	3	4	mean
0.1	0.740	102.7	99.6	98.5	102.0	100.7
0.25	1.86	103.7	102.7	102.7	101.1	102.6
0.5	3.71	101.9	102.2	101.2	101.7	101.8
1.0	7.42	100.1	100.6	101.5	101.9	101.0
1.5	11.1	100.2	101.1	100.8	101.6	100.9
2.0	14.8	101.4	101.4	102.5	100.8	101.5
RQL	0.330	94.1	96.1	94.1	93.4	94.4
1.0 (wet)	7.42	99.6	100.4	102.1	97.1	99.8

The stability of sample extracts prepared according to OSHA Method 5002 was examined by retaining the sample solvent extracts for the target concentration samples described immediately above. Two of the four vials were immediately recapped with new septa following the initial analyses, and again following each re-analysis event. The other two vials retained the original punctured septa throughout. All four vials were re-analyzed at 24, 48, and 72 hours after the initial analyses, with all vials remaining in an autosampler tray kept at 8.0 °C. Freshly prepared standards were used for each re-analysis event, and each septum (whether new or previously used) was punctured once for each injection. The resulting data are shown in Table H-6.

Table H-6. Extracted sample stability data for the polymeric 4,4’-methylenediphenyl diisocyanate 1-2PP derivative.

	punctured septa replaced recovery (%)		punctured septa retained recovery (%)	
time (days)	1	2	1	2
0	102.0	102.4	102.6	102.1
1	105.2	104.6	104.8	104.1
2	104.0	103.5	103.9	109.7
3	100.3	99.4	100.7	98.8

7 Sampler Capacity

The sampling capacity of a coated filter was tested by performing a sample media analyte retention test. A filter to be spiked was mounted within a cassette in front of another coated filter, with a spacer separating the two filters. Six coated filters were liquid spiked with polymeric 4,4’-methylenediphenyl diisocyanate 1-2PP derivative nominally two times the target concentration (calculated to be 0.927 mg/m^3). Air was drawn through these samplers with a flow rate of 1.0 L/min for 20 min. The relative humidity and temperature were 80% and 21.0 °C. Breakthrough was not observed after sampling for 20 min (corresponding to 20 liters). Data from six coated samplers, as shown in Table H-7, were used to determine the recommended sampling volume of 15 liters for polymeric 4,4’-methylenediphenyl diisocyanate as described in OSHA Method 5002. This volume corresponds to a 15 min sampling period, which is the maximum recommended sampling time regardless of breakthrough.

Table H-7. Retention data for the polymeric 4,4'-methylenediphenyl diisocyanate 1-2PP derivative.

sample no.	air volume (L)	recovery front (%)	recovery back (%)
1	20.0	96.4	0.0
2	20.0	98.1	0.0
3	20.0	98.8	0.0
4	20.0	98.6	0.0
5	20.0	97.4	0.0
6	20.0	100.0	0.0

8 Low Humidity

The effect of low humidity was tested by spiking six 1-2PP coated filters with the polymeric 4,4'-methylenediphenyl diisocyanate 1-2PP derivative in such a way that the mass of the derivative spiked was stoichiometrically equivalent to the mass of underivatized analyte that would be sampled at twice the target concentration (calculated to be 0.927 mg/m^3) in air for 15 min at a flow rate of 1.0 L/min. Following this, dry air (15.0% relative humidity at 21.0 °C) was drawn through each filter in a cassette at 1.0 L/min for 20 min. After immediate analysis, results as a percentage of expected recovery for the polymeric 4,4'-methylenediphenyl diisocyanate 1-2PP derivative were 102.6%, 102.2%, 103.5%, 101.4%, 103.0%, and 103.4%.

9 Chemical Interference

The effect of potential chemical sampling interference was tested by spiking three 1-2PP coated filters with the polymeric 4,4'-methylenediphenyl diisocyanate 1-2PP derivative in such a way that the mass of the derivative spiked was stoichiometrically equivalent to the mass of underivatized analyte that would be sampled at the target concentration (calculated to be 0.495 mg/m^3) in air for 15 min at a sampling rate of 1.0 L/min. Isophorone diisocyanate, methylene bis(4-cyclohexylisocyanate), and 1,6-hexamethylene diisocyanate homopolymer 1-2PP derivatives were also spiked at masses corresponding to sampling these as underivatized interferents under the same conditions at concentrations of 0.00500 ppm, 0.00562 ppm, and 0.601 mg/m^3 respectively. Following this, humid air (81.0% relative humidity at 22.0 °C) was drawn through each filter in a cassette at 1.0 L/min for 15 min. After immediate analysis, results for the polymeric 4,4'-methylenediphenyl diisocyanate 1-2PP derivative as a percentage of expected recovery were 100.1%, 100.4%, and 99.3%.

10 Analytical Method Reproducibility

Samples were prepared by spiking six 1-2PP coated filters with polymeric 4,4'-methylenediphenyl diisocyanate 1-2PP derivative in such a way that the mass of the derivative was approximately stoichiometrically equivalent to the mass of underivatized analyte that would be sampled at the target concentration in air for 15 min at a sampling rate of 1.0 L/min (calculated to be 0.499 mg/m^3). Following this, 15 L of humidified air (80.0% relative humidity at 21.0 °C) was drawn through each filter in a cassette. The resulting samples were submitted to the OSHA Salt Lake Technical Center for analysis using the procedures described in OSHA Method 5002 after ambient (22.0 °C) storage for 13 days. The analytical results corrected for E_E are provided in Table H-8. No sample result for the polymeric 4,4'-methylenediphenyl diisocyanate derivative fell outside the permissible bounds set by the precision of the overall procedure determined in Section 5 of this appendix.

Table H-8. Reproducibility data for the polymeric 4,4'-methylenediphenyl diisocyanate 1-2PP derivative (spiked and recovered μg/sample as the underivatized analyte).

spiked (μg/sample)	recovered (μg/sample)	recovery (%)	deviation (%)
7.49	7.01	93.6	-6.4
7.49	7.09	94.7	-5.3
7.49	6.93	92.5	-7.5
7.49	6.95	92.8	-7.2
7.49	6.95	92.8	-7.2
7.49	6.82	91.0	-9.0

11 Effect of Sampling a Low Concentration

A study has not been undertaken to verify the effect of sampling a low concentration of polymeric 4,4'-methylenediphenyl diisocyanate aerosol.

12 Estimation of Uncertainty

While systematic biases such as analyte storage loss are examined, and limits are placed on these, an estimation of uncertainty that encompasses both potential random and systematic error was not completed. Instead, the overall standard error of estimate was calculated from the random error inherent to the points about the regression line produced by the ambient storage test described in Section 5, as prescribed by the OSHA validation guidelines in use at the time OSHA Method 5002 was originally validated. See Section 5 of this appendix for details.

13 Controlled Test Atmosphere Procedure

A controlled test atmosphere containing polymeric 4,4'-methylenediphenyl diisocyanate aerosol was not generated.